ACUTE POISONING

A Review of 1,542 Patients Treated in 1964-65,

by

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Submitted as a thesis for
the degree of Doctor of Medicine

Edinburgh 1966

CONTENTS

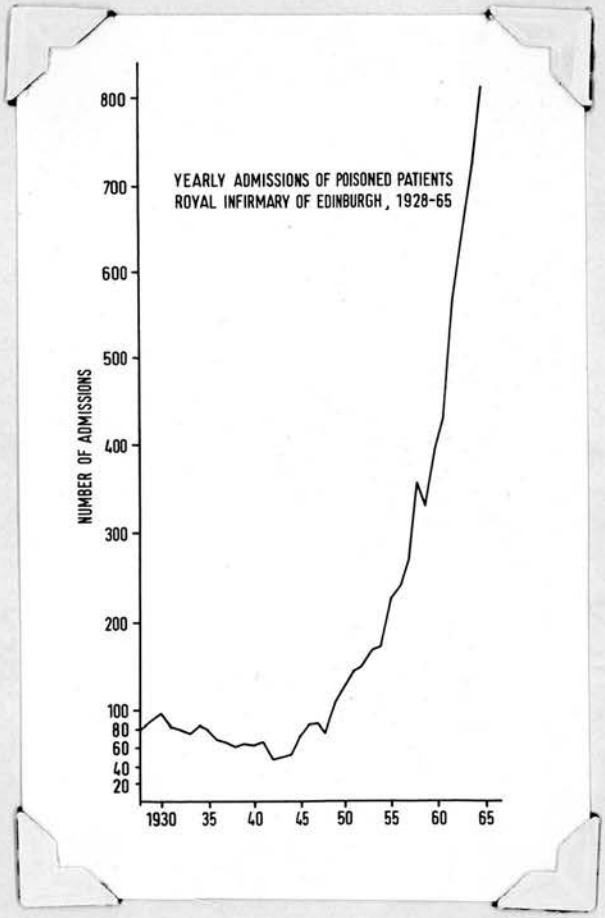
CHAPTER 1

INTRODUCTION

Historical: When the Royal Infirmary of Edinburgh moved from Infirmary Street to its present site in 1879 the provision was made for one ward to be set aside for patients suffering from incidental delirium. This condition occurring in the large Florence Nightin-:gale type of wards could be very distressing to other patients, hence should a patient in a general ward become unduly noisy or delirious he or she was transferred to Ward 3 where some extra pro-:vision was made for dealing with these patients. In addition to this function of Ward 3 it became recognised by doctors, police, ambulance workers and the public that poisoned patients would be accommodated therein. In the early years the number of poisoned patients was about 50 per annum, this figure remaining fairly con-:stant and being made up of patients who were truly suicidal. The commonest substances taken were lysol or arsenic, coal gas was also popular. Barbiturates, although introduced to medicine in 1903 as barbital (Veronal) and phenobarbital in 1912, accounted for only two instances of poisoning in 1936. With the advent of potent sedatives and tranquillisers available to treat noisy patients in the general wards the number of patients suffering from incidental delirium requiring transfer to Ward 3 steadily lessened and in 1965 amounted to no more than ten compared with the 120 of 1936. How-:ever, it happened that with the lessening in uncontrollable inci-:dental delirium the incidence of acute poisoning began to rise as

is shown in Fig. 1.

FIGURE 1



Poisoning Treatment Centres

In 1962 the Ministry of Health published a report "Emergency Treatment in Hospital of Cases of Acute Poisoning". This report was accepted in principle by the Scottish Home and Health Depart-:ment. An important recommendation of the report was that there should be set up district and regional poisoning treatment centres. Regional Hospital Boards in Scotland were requested to implement this recommendation. There are many cogent arguments in support

of special units for the treatment of poisoning (Matthew 1966). (1) Clemmesen (1963) demonstrated that in Copenhagen the mortality rate in hospital from poisoning was halved in the first year of central-:isation of treatment; (2) Unconscious poisoned patients admitted to a general medical ward may be suicidal. Unless special preven-:tive measures are taken they may be tempted to complete the act; (3) Suicidal and self-poisoned patients frequently experience feelings of guilt which may be expressed as aggressive behaviour. Doctors and nurses in general medical wards may not understand this behaviour in patients whom they regard as suffering from a self-inflicted ill-:ness. In special treatment centres understanding and confidence in handling such patients is soon acquired; (4) In such centres psychiatric advice is available on a 24 hour basis; (5) Clinical toxicology lags far behind other medical disciplines. The concen-:tration of patients in special centres would do much to advance knowledge rapidly.

In the South Eastern Region of Scotland the facilities available in Ward 3 of the Edinburgh Royal Infirmary already met the require-:ments, with one exception, of a regional poisoning treatment centre as defined in the report. The unit already had special accommoda-:tion, specially trained medical personnel and was adequately suppor-:ted by a psychiatric service. In addition, the expert advice of anaesthetists was readily available and an artificial kidney was located in the Infirmary. The exception was the lack of adequate laboratory support for toxicological examination of specimens from patients admitted to the Unit. This, however, was soon provided

by the Regional Hospital Board allocating funds for the establishment of a sub-unit in clinical toxicology in the University Department of Clinical Chemistry located in the Infirmary area.

The Poisoning Treatment Centre in the Royal Infirmary is the premier centre in Britain and thus affords a unique opportunity for the study of poisoned patients. No series incorporating the number of patients presented here has previously been described in the British literature.

This thesis is based on experience as Physician in Administrative Charge of the Poisoning Treatment Centre of the Edinburgh Royal Infirmary. The 1,524 poisoned patients admitted during 1964-65 provide the material for study.

CHAPTER 2

INCIDENCE OF ACUTE POISONING

The importance of acute poisoning as a common medical emergency is not fully appreciated. In many hospitals 10% of all medical admissions are due to acute poisoning (Curry 1965). The 1,542 admissions over the two years accounts for 11% of all medical admissions to the Royal Infirmary during that period.

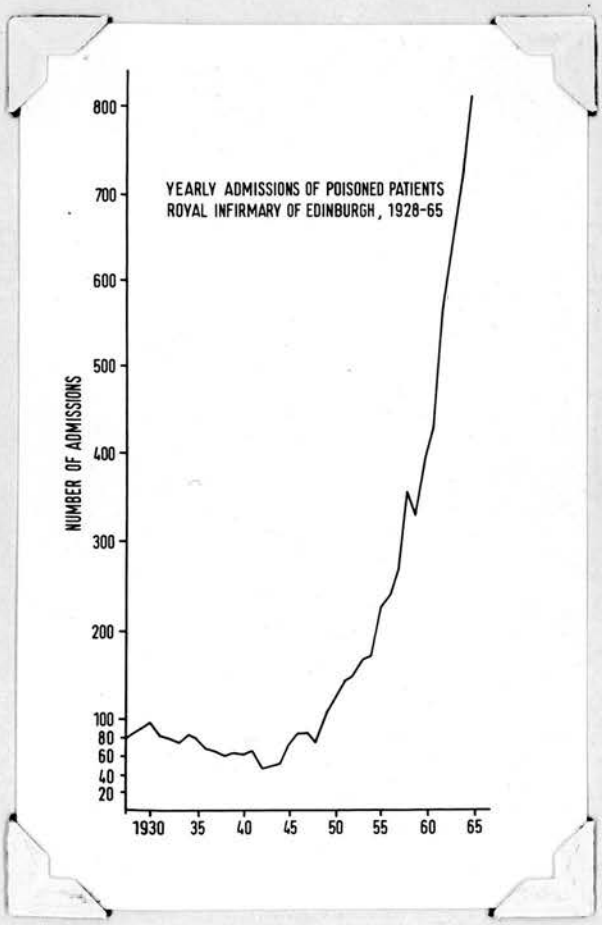


FIGURE 1

Fig. 1 shows the steep rise in the number of admissions, which, should it continue at the same rate, means that in 1984 the whole of

the population of Edinburgh will pass through the Poisoning Treatment Centre in that year! It is important to determine the cause of this alarming increase in incidence. Two types of poisoning are involved. The first and less important is the increase in incidence of domestic accidental poisoning.

Domestic Accidental Poisoning

Fatal domestic accidents are now a more important cause of death in developed countries than tuberculosis. (Backett 1965).

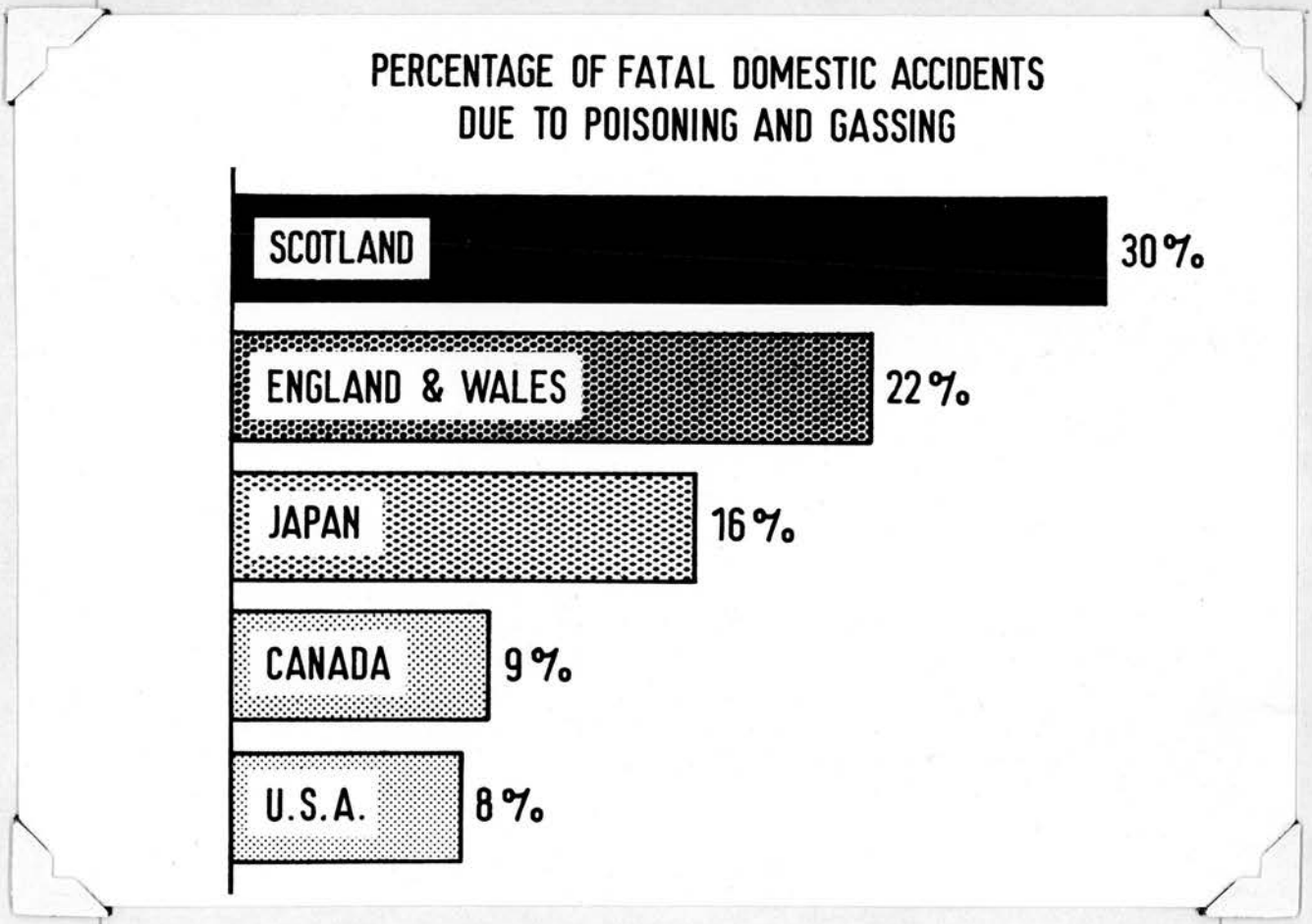
Table 1

RELATIVE IMPORTANCE OF DOMESTIC ACCIDENT MORTALITY AND TUBERCULOSIS MORTALITY IN A NUMBER OF COUNTRIES IN 1960

Country	Domestic accident deaths	Deaths from all forms of tuberculosis
Canada	2,235	823
Finland	451	1,263
Hungary	927	3,097
Ireland	140	468
Japan	6,343	31,884
Netherlands	1,294	325
New Zealand	258	84
Norway	594	229
United Kingdom:		
England and Wales	6,008	3,435
Northern Ireland	113	114
Scotland	1,048	509
United States of America	24,068	10,670
Venezuela	291	1,466

In 1960 twice as many patients died in Scotland from domestic accidents than from tuberculosis - 1,048 as against 509 (Backett 1965).

Of these domestic accidents a proportion will be due to poisoning and gassing, and Scotland, Fig. 2 holds the unenviable world position of being the country with the highest proportion, 30% as against 9% for Canada .



Self Poisoning

Despite this high incidence of accidental poisoning and gassing the major increase in poisoning has been shown by Kessel (1965) to be due to the increase in the numbers of patients suffering from self poisoning. The evidence is contained in Professor Kessel's Milroy lectures to the Royal College of Physicians of London in 1965. Professor Kessel's work for these lectures was undertaken when he was the psychiatrist attached to the Poisoning Treatment Centre in Edinburgh Royal Infirmary. The close collaboration which existed between Professor Kessel and the writer is acknowledged in the last paragraph of the published lectures - "Dr. Henry Matthew has given me a great deal of advice and help as we have thought through problems together. These lectures would be the poorer without the stimulus of his ideas, and I am deeply grateful".

Kessel drew attention to the increasing frequency of attempted suicide and advocated that it should be termed self-poisoning. He pointed out that it is often a conscious act, with little or no thought of self-destruction in mind. It is frequently impulsive and undertaken as a manipulative act to secure redress of some situation which has become intolerable. He emphasised that the sufferer usually takes care to prevent a fatal outcome by paying attention to dosage, and will often before losing consciousness announce to friends what he has done or even himself summon the police or ambulance in order to be taken to hospital. Once in hospital all the energies of the nursing, medical and psychiatric staff, together with those of the psychiatric social workers are expended on procuring the victim's recovery. The erring spouse

or boyfriend goes through a process of mourning to expiate his guilt and the intolerable situation which had precipitated the act is frequently righted. To call this behaviour attempted suicide is to attribute a frequently false motive to the act. Attempted suicide is neither a diagnosis nor a description of behaviour. In which direction lies success in attempted suicide? Is it death or favourable manipulation of the intolerable situation? The act is best designated self-poisoning. Unfortunately acci-:dents occur through misjudgement of dosage or of a failure to ensure that help would be available and an act committed merely to draw attention to a particular situation may result in death. Self-poisoning has become a recognised pattern of social behaviour and in Edinburgh one in every thousand of the adult population and one in every seven hundred teenage girls takes an overdose deliberately each year. There is a clear connection between self-poisoning and a broken home in childhood; alcoholism and poverty also play a part.

Eighty per cent of poisoned patients admitted to hospital will be suffering from self-poisoning. Genuine suicide is not commonly seen in the Poisoning Treatment Centre but some 10 per cent have deliberate self-destruction in mind. Accidental poisoning will also account for 10 per cent of admissions, but great care must be taken in making this diagnosis. For example, elderly depressed patients are frequently said to have poisoned themselves with coal-gas by accident, their impaired sight and sense of smell, together with poor physique contributing to the 'accident'. Such episodes are frequently examples of self-

:poisoning and it is not a real kindness to dismiss the incident as accidental when, in fact, the self-poisoning was committed as the result of a depression which requires urgent psychiatric treatment.

CHAPTER 3

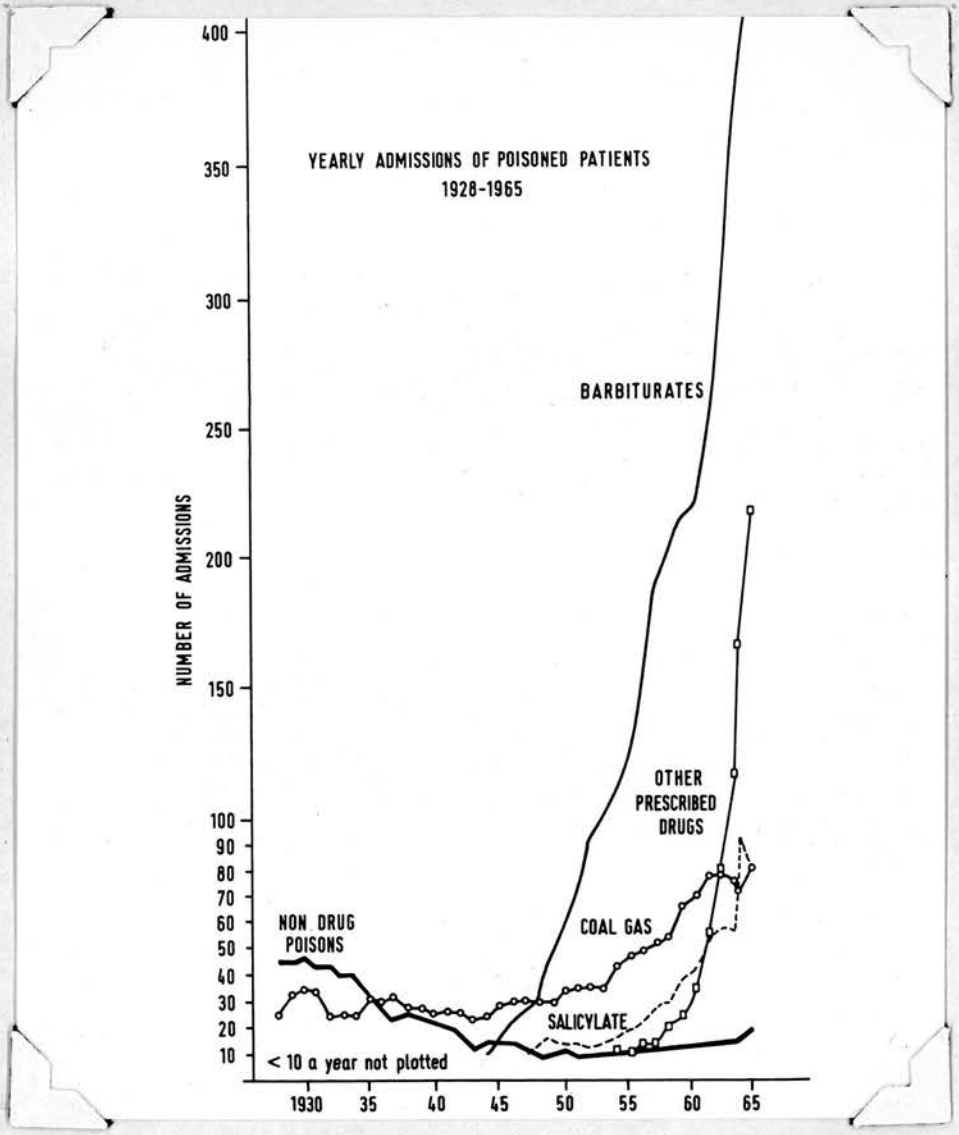
ADMISSION POLICY

It is dangerous to assume that because a patient has taken only a few tablets in excess of the therapeutic dose that his condition is proportionally the less serious. The size of the dose in no way parallels the severity of the underlying socio-:logical or psychological condition. On account, therefore, of this difficulty in assessment, all patients who had taken an over-:dose of drug were admitted. It naturally follows that a number of patients who are not really ill physically will be admitted. This situation has to be accepted and as there is psychiatric cover over the 24 hours these patients can be seen very quickly and their further management arranged. It has been estimated by Kessel et al (1964) that the Poisoning Treatment Centre of the Infirmary catered for over 90% of poisoned patients admitted to hospital in Edinburgh, it should therefore be possible to establish a clear picture of acute poisoning in a population of 400,000.

CHAPTER 4

DRUGS INVOLVED IN SELF POISONING

Fashions change in the selection of drug or other means of self-poisoning as is shown in Figure 2a.



The favourite group of drugs is obviously the barbiturates but under 'other prescribed drugs' is included tranquilliser, anti-depressive and other hypnotic drugs. It may well be that this group, prescribed for the very people who are likely to indulge in self-poisoning, will rapidly become more popular at the expense of

the barbiturates. The ready availability of drugs from the Health Service since 1948 has been blamed by some for the rapidly rising incidence of self-poisoning, but asprin poisoning has also increased since 1948 and of the 4,000,000,000 tablets of salicylate preparations consumed yearly in Britain much less than half are procured on prescription. Several different drugs may be taken at one and the same time in the act of self-poisoning and alcohol is also frequently involved. The choice of method also varies with age.

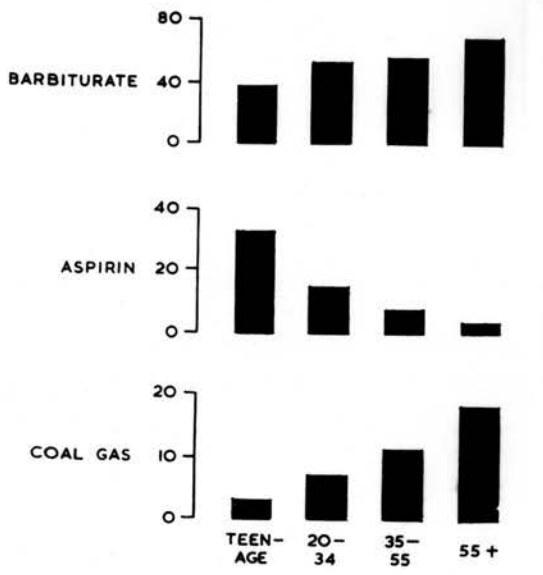


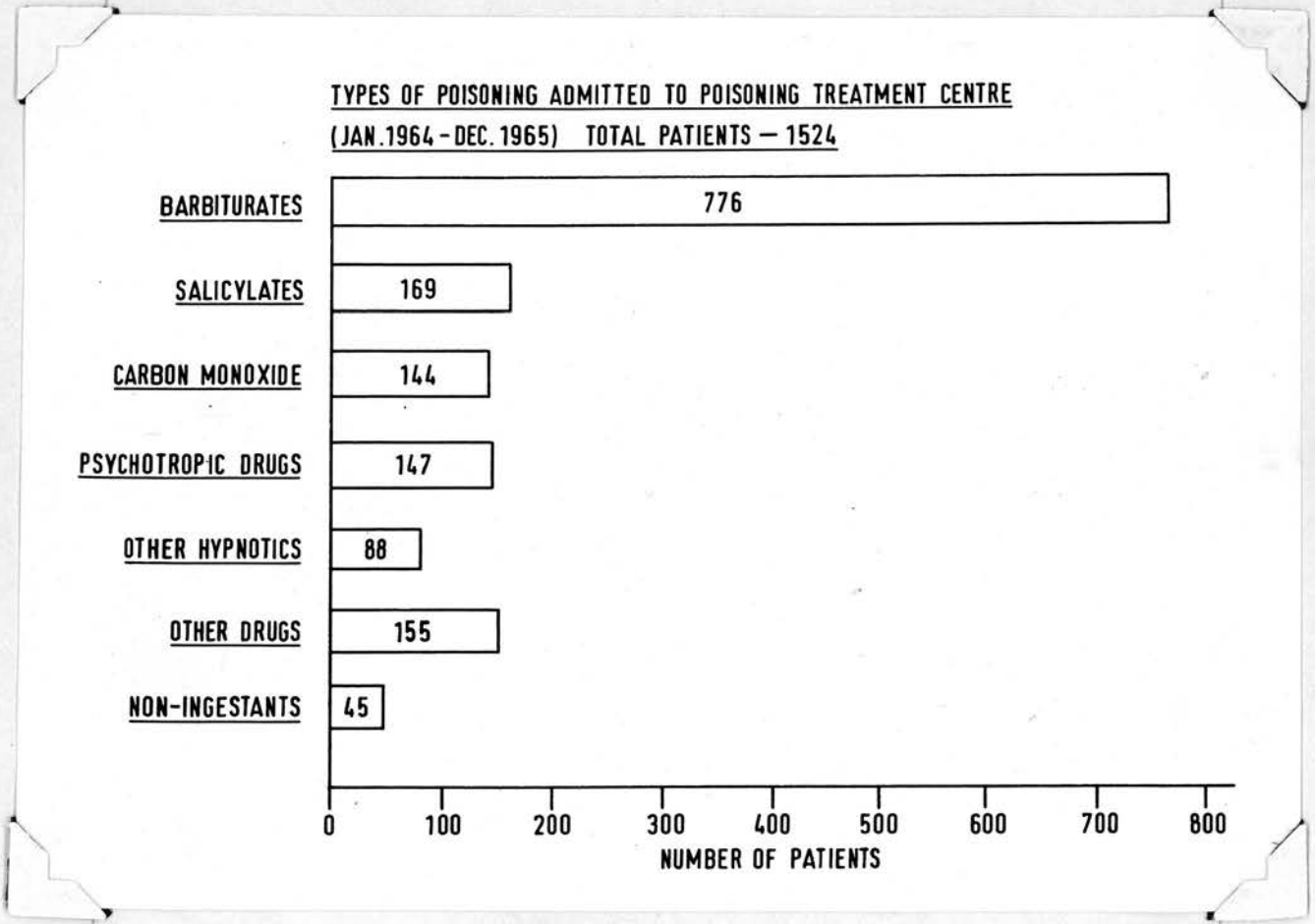
Fig. 3. Methods of self-poisoning used at different ages.

Fig. 3

Figure 3 shows clearly how asprin is the choice of the teenager and that elderly people have a marked preference for coal-gas.

The drugs taken by the 1,524 patients admitted during 1964 and 1965 are shown in Fig. 3a, the breakdown being simply into the major groups. More detailed information regarding "other hypnotics" and "other drugs" will be found under the sub-headings for these drugs in the later sections.

FIGURE 3a

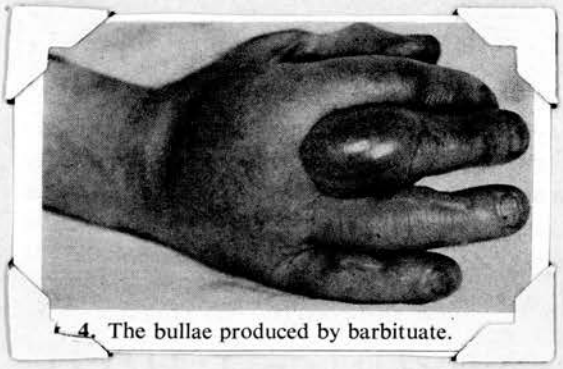


CHAPTER 5

DIAGNOSIS OF ACUTE POISONING

The circumstantial evidence may be so apparent that there is no doubt that the patient has taken poison. This is most evident in instances of self-poisoning when the patient intimates what he has done prior to losing consciousness. It may also be equally evident in the suicide who takes precautions such as ensuring that the gas cannot escape from the room and who frequently leaves a suicide note. Few poisons produce specific diagnostic features although the smell of coal gas associated with the pink discoloura-:tion of the skin will make this diagnosis self evident. The pin point pupils, depressed respiration and vomiting evident in poisoning by morphine and related alkaloids will be of help in diagnosis, as will the flushing, sweating, tinnitus, deafness and tachycardia of salicylate poisoning. The diagnosis of poisoning, if not apparent from the circumstantial evidence and the few diagnostic features just mentioned, will be made on the unconscious patient by excluding other causes of loss of consciousness. In such patients the find-:ing of blisters on the skin often occurring on an area of erythema strongly suggests barbiturate as the cause of the coma.

Barbiturate Blisters



4. The bullae produced by barbituate.

The bullae, Figure 4 produced by barbiturate, first described by Holten (1952), have again been brought to notice by Beveridge and Lawson (1965) working in my Unit. They demonstrated this lesion in 7 per cent of patients admitted with barbiturate poisoning and suggested that the finding of such lesions in an unconscious patient indicates that the patient is probably suffering from acute barbiturate poisoning. Blisters or lesions of similar appearance have also been recorded in glutethimide poisoning, but were not seen

in any of our 25 patients suffering from this form of poisoning. Bullae occurred in one patient who had taken ethchlorvynal and whose blood barbiturate and glutethimide levels were zero. These lesions should not be confused with the necrotic blisters seen in carbon monoxide poisoning.

The mechanism of production of the blisters is uncertain but they are not solely due to pressure. Histologically the picture resembles that of toxic epidermal necrolysis, Lyall's disease (1956). We have found that the blister fluid contains barbiturate in a concentration less than that in the serum. The possibility of a relationship with acute porphyria is currently being investigated.

CHAPTER 6

IDENTIFICATION OF POISON

The identification of the substance taken is often said to be of prime importance. As will be seen when treatment is discussed antidotes are extremely few, hence in practice the treatment is not the administration of the appropriate pharmacological antagonist but the adoption of basic therapeutic measures. Frequently the half empty bottle brought with the patient by the police or the sorrowing relatives is not necessarily that from which the tablets have been taken. Moreover several drugs may have been taken at any one time. Valuable time at the outset should therefore not be spent in endeavouring to identify the drug taken. When the emergency treatment of the patient has been completed then identification should be undertaken, the coloured charts available in "Medinex" or the "Chemist and Druggist" being of some help in this respect as also is the recent introduction of marking tablets with a code letter and number. The only certain identification of the poison will however be determined by laboratory testing.

We routinely undertake the estimation of serum salicylate by Trinders method (1954) in the Ward side room and the method of Curry (1964) for the rapid estimation of blood barbiturate levels is also carried out in the Ward. The results are cross-checked by the laboratory. We have found that in salicylate poisoning accurate estimation is comparatively easy to achieve but with barbiturates the results do not always correspond closely to those obtained by ultra violet spectrophotometry in the laboratory.

CHAPTER 7

MANAGEMENT OF ACUTE POISONING

(a) Antidotes

It is still widely but erroneously believed that for each toxic substance there is a specific antidote. In this series in less than 1% of instances was a pharmacological antagonist available. The treatment of acute poisoning is clearly, therefore, not the application of the appropriate antidote but is the adaption of basic therapeutic principles. These basic principles are now discussed under their separate headings.

(b) Gastric Aspiration and Lavage

The prevention of further absorption of the poison by gastric aspiration and lavage was evident to us as a problem which required clarification. We therefore decided to study it in some detail.

There is no doubt that in certain types of poisoning gastric aspiration and lavage is positively dangerous, thus this form of therapy has no part to play in the management of poisoning by Kerosene and other petroleum distillates (Capel et al 1960, Cachia et al 1964, Baldachin et al 1964). It should be undertaken with the greatest of care when corrosive poisons have been swallowed, also in the elderly and very young and in patients who have had gastric surgery. However, the majority of adult poisoned patients seen in hospital in this country do not fall into these limited groups and surprisingly the advice offerred by various authors is contradictory as to the value of gastric aspiration and lavage, particularly with regard to barbiturates which are by far the commonest

drugs taken by adults.

Historical

The most important paper in this field was written by Harstad et al in 1942, and as these workers' findings have influenced every author since that time it is necessary to study closely both their results and analytical methods. They investigated 71 cases of barbiturate poisoning. In 40 lavage with 10 litres of water re-:covered no barbiturate. Less than 100 mg. was recovered in 86% of cases and in only 3% was more than 500 mg. of barbiturate re-:covered. They suggested that absorption of the drug was, in fact, increased by this procedure because barbiturate was washed into the small bowel and they could find no correlation between the amount of barbiturate ingested, the time interval between ingestion and washout, and the amount of barbiturate recovered. Furthermore, the finding of charcoal (added to the lavage fluid) in the lungs of patients who died demonstrated the dangers of the procedure. In view of these dangers and the poor quantities of drug recovered these authors concluded that in no instance could the stomach washout have any therapeutic value and advised abandonment of stomach washout in barbiturate poisoning. Their methods of chemical analysis in-:volved extraction followed by the isolation of the substance under investigation by crystallisation. Identification was then made by the determination of the Melting Point. Quantitation was made by weighing the purified substance prepared for the Melting Point deter-:mination. Such a procedure does provide an excellent means for identification purposes but is of little value for quantitation

owing to the extremely large losses involved.

During the 23 years since Harstad's paper was published, there have been great technical advances in the methods of analysis as applied to chemical toxicology. New instrumentation, e.g. U.V. spectrophotometry, has been introduced which allows much more reliable quantitation. Harstad's recommendation based on what is now known to be inaccurate measurement of the amount of drug re-:covered has, however continued to be quoted as evidence against gastric lavage. This, along with their demonstration that particles of charcoal added to the lavage fluid could later be found in the pulmonary tissues of those patients who died led to the abandonment of gastric lavage by Danish workers (Louw 1958), and the undertaking of gastric aspiration alone without lavage if it was known that the drug had been taken within one hour previously (Clemmesen et al 1961). However, Wright (1955) found that in three out of six patients treated within four hours of ingestion appreciable quanti-:ties i.e., over 200 mg. of barbiturate were recovered from the gastric washings. In the six patients treated more than four hours after ingestion no barbiturate was recovered.

Allan (1961) recording his experience with 68 patients, stated that "in most cases of barbiturate overdose, stomach lavage removes only small quantities of ingested barbiturate". He stressed the hazards associated with the procedure especially in inexperienced hands when the patient was semiconscious. He encountered no com-:plications in conscious patients and deeply unconscious patients with endotrachael intubation "posed no problems". However, he concluded that "routine lavage of the stomach of patients unconscious

as a result of barbiturate overdose should be regarded as potentially dangerous in all cases and of no value in most". He did not however, give any criteria as to when the procedure might be of value.

The practitioner is thus understandably confused by the advice offered by various authorities; some textbooks (Cecil-Loeb, 1963) only advocate lavage within four hours of ingestion of barbiturate, other authors within 8 hours, (To-day's Drugs Brit. Med. J. 1964) (Graham 1962), and some almost irrespective of the time since inges-:tion (Deichmann et al 1964, Davidson 1964). Clemmesen et al (1961) and Mark & Papper (1964) employ gastric aspiration alone, without lavage, and that only if the patient is seen within one hour of in-:gestion of the barbiturate.

In view of the paucity of accurate information on this subject and the divergence of opinion regarding the value of gastric aspira-:tion and lavage in acute poisoning, as already stated, it was deci-:ded to carry out a study on poisoned patients admitted to the Poison-:ing Treatment Centre.

Method

During a five month period of 1965 gastric aspiration and lavage was carried out in all patients admitted to the Poisoning Treatment Centre who had ingested drugs of poison of any type. There was no case of kerosene poisoning.

In all conscious patients and in unconscious patients with in-:tact cough and gag reflexes a large bore stomach tube (Jacques, Eng-:lish gauge 30) was passed. If the patient was unconscious with absent pharyngeal and laryngeal reflexes, protection of the lungs and patency of the airway was secured by inserting a cuffed endro-

:tracheal tube before passing the stomach tube.

Following passage of the stomach tube aspiration of the gastric contents was carried out with the aid of a Senoran's evacuator. If no contents could be aspirated, 100 ml. of water was introduced into the stomach and the fluid aspirated. This initial aspiration speci-:men was sent for analysis. Gastric lavage was then performed using no more than 300 ml. warm water for each single washout. A total of 2 litres was usually required before the returning fluid was clear but on occasions when large amounts of food or drug were evident as much as 7 litres was employed. An aliquot of the wash-:ings was sent for analysis.

Biochemical Methods

The methods employed in this investigation were:-

1. Barbiturates were estimated by U.V. spectrophotometry (Unicam spectrophotometer, S.P. 800) Curry (1964)
2. Aspirin was converted into salicylate by mild alkaline hydrolysis and then determined as such by the Trinder method (1954).
3. Other substances were estimated by conventional methods or modifications of such using modern instrumentation such as U.V. spectrophotometry.

Results

From April 1st until August 31st 1965 gastric aspiration and lavage was performed on 254 patients who had ingested poison and were admitted to the poisoning Treatment Centre. Although a variety of different drugs and other substances had been ingested, 65% of the patients had taken barbiturate in some form (Table 11)

TABLE 11 Substances taken by 254 patients (in a number of instances more than one substance had been ingested)

	Total	No. in which gastric contents were analysed
Barbiturates	165	148
Salicylates	25	22
Librium (chlordiazepoxide)	13	11
Largactil (chlorpromazine)	11	6
Tryptizol (amitryptiline)	9	5
Amphetamine	7	2
Chloral & Welldorm (dichloralphenazone)	7	5
Doriden (glutethimide)	6	5
Equanil (meprobamate)	3	3
Epanutin (phenytoin)	3	1
Panadol (paracetamol)	2	2
Tofranil (imipramine)	2	2
Melleril (thioridazine)	1	1
Arvynol (ethclorvynol)	1	1
Noludar (methyprylone)	1	1
Pethidine	1	1
Acetarsol	1	1
Ephedrine	1	1
Miscellaneous:	Disinfectant (2) Varnish (2) DF118 (2) Ferrous Sulphate (2) Pro-Plus (1) Trinitrin (1) Pernivit (1) Oblivon (1) Warfarin (1) Alcohol (1) Potassium Bichromate (1) Antacid tablets (1) Ergotamine (1) Scheriproct (1) Alophen (1) Unknown (1)	

Whenever possible the stomach contents recovered by gastric aspiration and lavage were analysed but some were not examined for the following reasons:

1. Suitable methods were not available for identification or quantitative determination.
2. When two or more drugs had been taken it was sometimes only possible to analyse the washings for the more important.
3. Specimens were lost, broken, inaccurately or wrongly label-

:led: seventeen of the barbiturate cases were not analysed for this reason (Table 11).

The results obtained in the patients suffering from barbiturate or salicylate poisoning are given in detail below and the less com-:mon drugs are mentioned briefly later.

Patients Poisoned by Barbiturates

The gastric aspirate and washings were analysed in 148 out of 165 patients suffering from barbiturate poisoning (92%) and more than 200 mg. of barbiturate was recovered in 25 (17%). In 130 patients the time interval between ingestion and washout was known with reas-:onable accuracy and in Table 111 and Fig. 5 the total amount of barbiturate recovered from the aspirate and lavage is related to this time interval.

TABLE 111 Barbiturate Recovery in Relation to Time

Time (hours)	0-4	4-8	8-12	12-24	24 +
No. of patients	65	26	12	23	4
No. in whom more than 200 mg. barbiturate recovered.	24	1	-	-	-

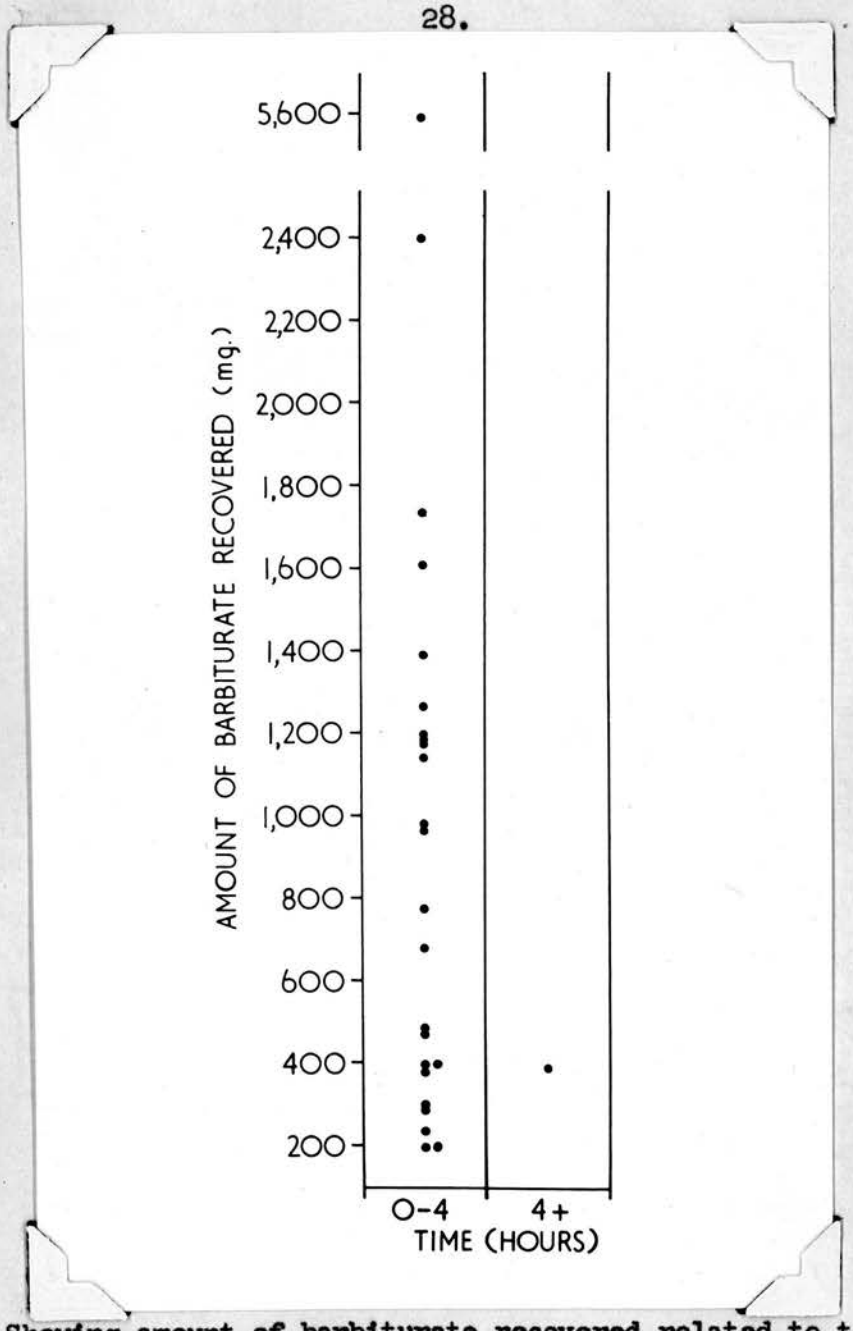
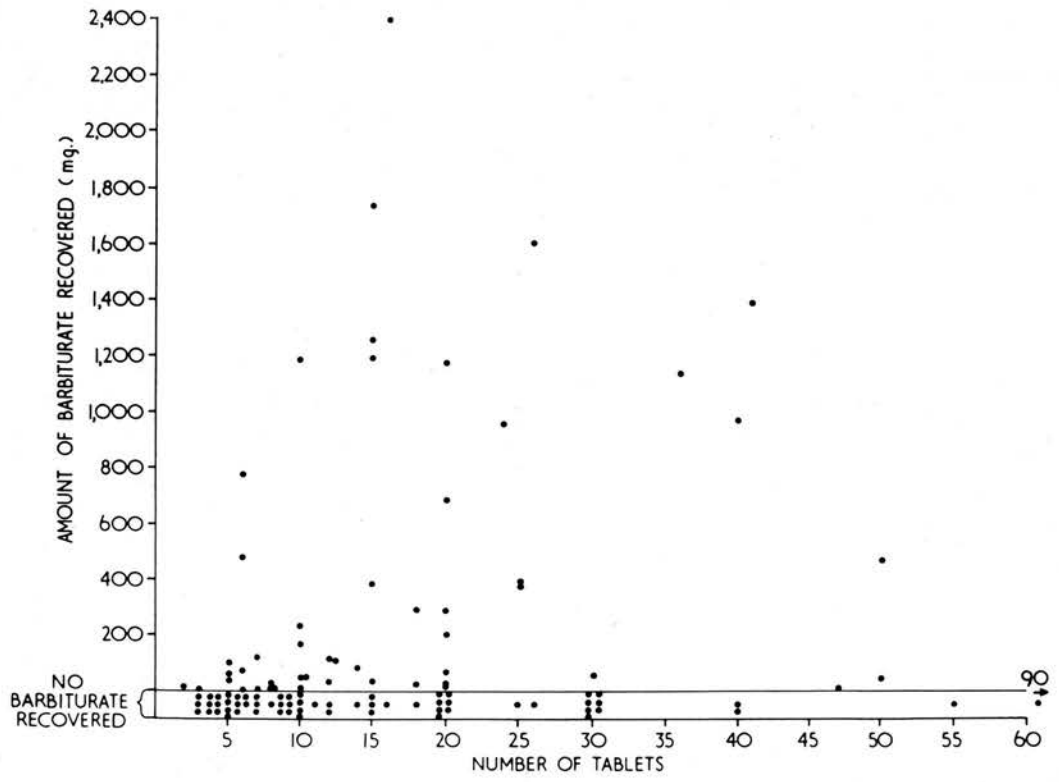


Fig. 5 Showing amount of barbiturate recovered related to time interval since ingestion.

In 111 patients the number of tablets or capsules taken could be ascertained and in Fig. 6 the amount of barbiturate recovered in the washings is related to the number of tablets taken. Seldom can one discover with any degree of accuracy the strength of the tablets or capsules incriminated, hence, "number" is plotted irrespective of strength.

FIGURE 6



In 109 patients both the time interval and the number of tablets or capsules taken were known and Table IV shows the relationship between the amount of barbiturate recovered, the number of tablets taken and the time between ingestion and washout.

TABLE IV Relation between barbiturate recovered, the number of tablets ingested and time.

	Under 4 hours				Over 4 hours			
No. of tablets	0-10	11-20	21-50	51 +	0-10	11-20	21-50	51
No. of patients	24	24	11	-	26	11	11	2
No. of patients whom 200 mg. or more barbiturate recovered.	4 (17%)	9 (37.5%)	8 (73%)	-	-	1 (9%)	-	-

In Fig. 7 the amount recovered is related to the level of consciousness of the patient, the grades of unconsciousness being defined as follows:-

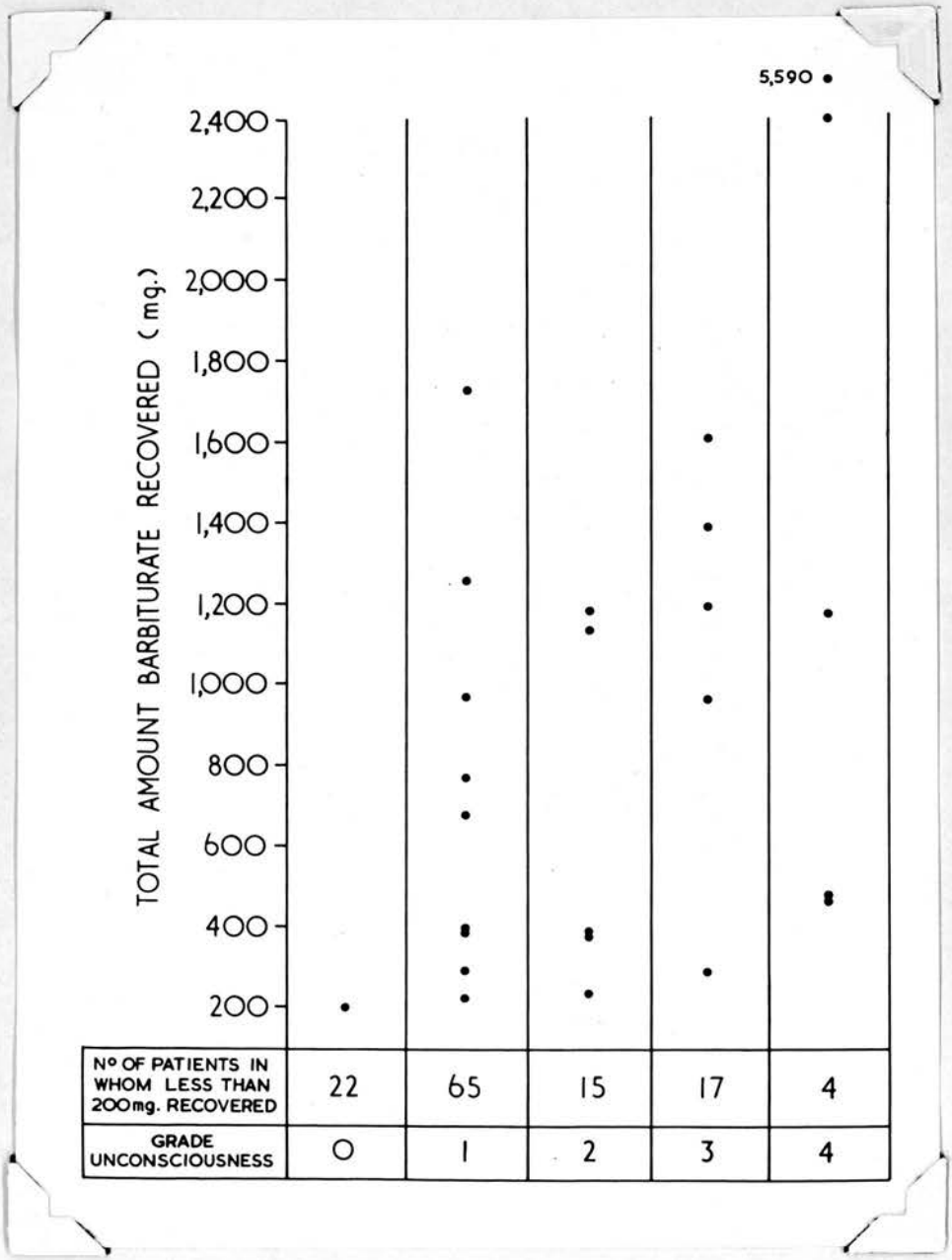
Grade 0 - Fully conscious.

Grade 1 - Drowsy but responds to vocal command.

Grade 2 - No response to vocal command. Maximum response to minimal painful stimuli.

Grade 3 - Minimal response to maximal painful stimuli.

Grade 4 - No response to painful stimuli.



Patients Poisoned by Salicylates

In salicylate poisoning the patient is almost always conscious, as were all 25 in this study. Table V shows the amount of salicy-:late recovered by gastric aspiration and lavage in these patients, together with the time interval since ingestion. The blood salicy-:late on admission is also shown.

TAVLE V Details of patients poisoned by Salicylates.

Drug and No. Taken	Time between S.W.O. and ingestion (hrs)	Amount salicy-:late recovered (mg.)	Blood salicy-:late (mg.)
Aspirin x 200	9	20,340	67
Aspirin x 50	8	5,100	41
Codis x 30	¾	4,966	12
Codis x 46	2¾	1,753	19
Aspro ? No.	?	1,525	23
Codis x 14) Anadin x 20)	4	1,312	51
Aspirin x 80	5½	790	25
Aspirin x 67	5	575	57
Edrisal x 20	2½	458	13
Aspirin x 40	1¼	444	26
Aspirin x 50	1½	408	47
Aspirin x 24	6	374	45
Aspirin x 15	2¾	368	21
Doloxene x 20	2	242	
Aspirin x 7	2½	114	12
Aspirin x 150	13	68	95
Aspirin x 24	14½	54	27
Aspirin x 40	9	34	34
Aspirin ? No.	24	22	10
Alkaseltzer x 15	3	Nil	-
Aspirin x 15	24	Nil	34
Aspirin x 50	12	Nil	70
Tercin ? No.	3½	Nil	25
Codis x 6	3½	Not estimated	14
Salicylates ? No.	?	Not estimated	5

Conclusions

It seemed logical to us that gastric aspiration and lavage would be of some value if the procedure could be undertaken quickly enough after the ingestion of the drug and that there should be little danger from the procedure if the lungs were protected by a cuffed endotracheal tube in those patients in whom the pharyngeal and laryngeal reflexes were absent.

We think that this assumption is substantiated by our results in barbiturate poisoning. We consider that 200 mg. or more of barbiturate is a worthwhile recovery and we have shown (Fig. 5) that amounts far in excess of this figure (e.g. 5.5 g.) can be obtained by stomach washout.

However, this is only achieved when the patient is washed out within four hours of taking the drug and this time interval is by far the most important factor in determining the amount of barbi-:turate recovered. The number of tablets ingested has no direct relationship to the amount of barbiturate recovered (Fig. 6), but when account is also taken of the time since ingestion, then there is a correlation between the number of tablets taken and the amount recovered (Table IV).

In those patients who were washed out within four hours of taking the drug, more than 200 mg. of barbiturate was recovered in 73% of those taking more than 20 tablets, in 37.5% of those taking 11-20 tablets but in only 17% of those ingesting under 10 tablets. Thus, within the time limit of four hours the value of the proced-:ure is also as would be expected, related to the number of tablets ingested.

In patients suffering from barbiturate poisoning who are deeply unconscious bowel sounds are often absent on ausculation of the abdomen (Schreiner, 1958) and under these circumstances absorp-:tion stops. Thus the best results from gastric washout may be obtained in the deeply unconscious patient about whom little infor-:mation is available on admission. This is also confirmed by our results. More than 200 mg. of barbiturate was recovered in 55% (5 out of 9) grade 4, 23% (5 out of 22) grade 3, 25% (5 out of 20) grade 2, and only in 12% (9 out of 74) grade 1 unconscious patients. In only 1 out of 23 conscious patients was more than 200 mg. of barbiturate ever recovered, presumably because these patients had taken so few tablets. In those grade 4 patients who were washed out within four hours of taking the drug, more than 200 mg. of bar-:biturate was recovered in 5 out of 6.

We have found that the aspirate always contains a higher concentration of barbiturate than the washings, but the total re-:covery of barbiturate will be much greater in the washings than in the aspirate, especially if the latter is only of small volume.

Many patients with barbiturate poisoning will not benefit from gastric aspiration and lavage and the problem is to decide which patients should receive this treatment. We would suggest that patients who fulfil the following criteria should be washed out:-

1. Those who ingested the tablets or capsules within four hours unless it can be definitely established that fewer than ten were taken.
2. If the time of ingestion is not known and the patient

is unconscious.

The other hypnotics, tranquillisers and drugs for mental state are not discussed here in detail but in general we would suggest that the same criteria for stomach washout should be applied as for barbiturates.

Salicylates do not appear to behave in the same way as barbiturates in that they remain in the stomach for longer periods (Rushton, 1963. Beveridge et al 1964) and large amounts salicylate can be recovered many hours after ingestion (Table 5). One patient in this series ingested 200, 5 gr. tablets (60 g.) nine hours prior to admission and 20 g. of salicylate were recovered in the gastric washings. These patients are conscious, thus gastric aspiration and lavage does not have the same risk as in the unconscious patient. We would advise gastric aspiration and lavage in all patients poisoned with salicylate irrespective of the time since ingestion.

Gastric aspiration and lavage does have risks but we feel that these are frequently overemphasised, for instance, we have never observed cardiac arrest as a result of the procedure (Lee & Ames 1965).

Perforation of the oesophagus has occurred once in our experience in the last two years. This patient was an elderly chronic alcoholic who was drunk and poisoned by barbiturate. However, aspiration of fluid into the lungs with the development of pneumonia can occur. Eight patients (3%) in this series developed a complication which could possibly have been a result of the gastric aspiration and lavage, (Table VI). Two of these were definitely related to the stomach washout, but the relation of the remaining 6 to the

procedure is probably fortuitous as infection may develop prior to admission, (Mackintosh & Matthew 1965).

TABLE VI Respiratory Complications developing in eight of the 254 Poisoned Patients

Sex	Age	Drug	Grade of Uncons.	Time between ingestion & S.W.C.	Complications	Remarks
M	45	Nembutal x 16	4	1½	R. basal pneumonia	E.T. Intubation. Infection developed 20 hrs. after admission. Unconscious 59 hours. Peritoneal dialysis.
M	26	Tuinal x 20	4	2	Consolidation R.L.L. on X-ray Clinically nil.	E.T. Intubation. Aspirated vomitus 20 hrs. after S.W.O. following accidental removal of endotracheal tube. Peritoneal dialysis
M	34	Sodium Amytal x 24	3	1½	No infection.	Became cyanosed whilst being washed out and required intubation
M	48	Sodium Amytal x 8	1	½	Collapse L. Lung	Become cyanosed whilst being washed out. Bronchoscopy.

TABLE VI (Cont.)

Sex	Age	Drug	Grade of Uncons.	Time between ingestion & S.W.O.	Complication	Remarks
M	33	Pneobarbitone x 12 Equanil x 20 Theobromine	1-3	3½	R. basal pneumonia	Infection first observed 4 hours after admission. Unconscious 36 hours. Drowsy on admission but became grade 3.
M	36	Tryptizol x 50 Librium x 29	3	5	R. basal pneumonia	Aspirated vomitus 8 hours after S.W.O.
F	31	Welldorm x 20 Librium x 12	1	2	Clinically nil, X-ray: Broncho-pneumonic consolidation in the anterior & lateral basal segments of the R.L.L.	———
F	19	Sodium Amytal x 90	2	?	Clinically nil, X-ray: Diffuse opacity R.L. zone suggesting a pneumonic process	———

We regard this figure of 3% as acceptable in view of the value of gastric aspiration and lavage. Selection of patients using the criteria for washout that we suggest, together with efficient protection of the lungs whenever necessary, should reduce the complication rate to a negligible figure. In the deeply unconscious patient a cuffed endotracheal tube should always be inserted prior to passing the stomach tube. If this cannot be done the procedure should be abandoned.

(C) Respiratory Failure

Respiratory obstruction is frequently a cause of death and morbidity in poisoned patients. It is imperative that the airway be cleared of debris and vomit and the patient placed in the lateral position during transport to hospital and until recovery of consciousness. An oropharyngeal tube should be inserted to maintain a clear airway. Artificial respiration may be required. In hospital an assessment of respiratory efficiency can be obtained by measuring the minute volume with a Wright's spirometer. In practice a reading of less than 4 litres per minute indicates that measures must be taken to improve ventilation. Often a short period of hand ventilation using a Water's canister is sufficient, but in more severe respiratory failure a mechanical respirator may be required. Oxygen should be given by polymask or if there is CO_2 retention by Edinburgh mask. The injection of respiratory stimulants such as nikethamide is of little value other than as a temporary supportive measure while other methods to maintain respiration are being prepared.

(d) Prevention of Respiratory Infection

Conflicting views as to whether prophylactic penicillin should be employed in unconscious poisoned patients were evident. We therefore decided to study the problem in some detail.

Historical

For many years textbooks of medicine and therapeutics (Cecil & Loeb 1959, Birch 1963, Davidson 1964 Current Therapy 1965) and published work on this subject such as that of Cumming 1961 and Graham 1962 have advised giving prophylactic antibiotics, especially penicillin, to these patients. One textbook (Dunlop et al 1964) recommends prophylactic penicillin for the unconscious poisoned patient, but elsewhere states that in the management of coma, penicillin prophylaxis may be positively dangerous. Prophylactic therapy is intended to ward off respiratory infection, but there is little evidence to show whether the unconscious poisoned patient is in fact prone to respiratory infection, or whether antibiotics can prevent it. Petersdorf and his colleagues (Petersdorf et al 1957, Petersdorf 1961, Petersdorf et al 1961a, Petersdorf et al 1961b) demonstrated that their use may even expose the patient to danger.

Plum and Swanson (1957) gave penicillin prophylactically to 123 patients comatose from barbiturate poisoning, and attributed the low mortality (2.5%) partly to its effects. But the usual mortality in barbiturate poisoning, under similar conditions, is of the order of 2-3%, hence the assertion that antibiotic propy-:laxis contributed to the low mortality is questionable. Clemmesen

and Nilsson (1961) give routine antibiotic prophylaxis, but they have not claimed that it directly improves mortality (1-2% in their series) or morbidity.

Petersdorf and others (1957) studied 72 patients suffering from other causes of coma, mostly cerebral vascular accidents. Half of these patients had antibiotics prophylactically, and the others had none. There was no difference in mortality, but pulmonary infec-:tions were commoner in patients receiving antibiotics (50%) than in those not receiving them (15%), and also more serious. Other infections occurred only in those receiving antibiotics. All pa-:tients who were catherised developed urinary infections despite drug prophylaxis. 85% of the patients ultimately had Staphylococcus aureus in the anterior nares and nasopharynx, although it had been present in only a few cases on admission. Gram-negative organisms were isolated from 88% of patients receiving prophylaxis but only from 50% of the others. Petersdorf et al concluded that "prophy-:lactic antibiotic therapy is of no benefit and is distinctly hazardous in unconscious patients".

Weinstein, (1955) in a study of respiratory distress associated with poliomyelitis, found that "prophylaxis failed to protect those who were in need of the greatest protection", and that its use had been based mainly on clinical impression, rather than on fact.

Studies of bacterial implantation in patients with tracheosto-:mies (Leper et al 1954) and of postoperative chest infection, (Griffiths 1957, Thulbourne et al 1962) have also failed to confirm the value of antibiotic prophlaxis.

Thus, despite the advice in textbooks, there is no evidence that penicillin or other antibiotics alone or in combination can prevent chest infection in unconscious patients. Moreover, resis-:tant organisms appear more frequently when these drugs are used, and no single antibiotic can prevent bacterial implantation. Two or more drugs in combination may possibly delay it, but the organ-:isms which are then ultimately implanted are usually highly resis-:tant.

We therefore decided to re-examine the problem. We chose un-:conscious poisoned patients for the trial because they could nor-:mally be expected to recover. In most other investigations the differing causes of the unconsciousness have made a uniform study difficult. Poisoned patients are a relatively uniform group, with the one inherent disadvantage that they do not remain unconscious for as long as patients suffering from such states as cerebral vas-:cular accidents. We investigated the infection-rate in unconscious poisoned patients, and the prophylactic value of penicillin against respiratory infection. We studied 177 consecutive unconscious patients admitted to the Poisoning Treatment Centre during a period of fifteen months.

Method

We regarded as unconscious a patient who was unable to reply to simple questions after, if necessary, preliminary stimulation by pain. All poisoned patients who were unconscious on admission were included in the trial unless:

1. They were already suffering from respiratory infection.

2. They had aspirated vomitus or food.

3. Treatment had already been started elsewhere.

4. They had, in addition, other disorders such as diabetes, were on steroid therapy, or were penicillin-sensitive.

144 patients were admitted to the trial and divided at random into two groups. The control group (71 patients) had no prophylaxis, and the "treated" group (73 patients) received penicillin.

All the "treated" patients were given crystalline penicillin 2 million units intramuscularly twice daily until they had been conscious for 24 hours. A physician who did not know whether the patient was receiving penicillin or not examined all the patients for signs of respiratory infection at least once daily whilst they were unconscious, and 24 hours after consciousness had returned. A chest X-ray was performed within 8 hours of admission, and on the third day or later if it had not already had to be repeated. The criterion of respiratory infection was the presence of a local or generalised pulmonary lesion, determined by physical signs or chest X-rays, which had not been present on admission.

Patients excluded from the trial also had the standard proforma filled in, and were observed in the same way as patients in the trial for the development of respiratory infection.

Any chest infection that developed was treated conventionally. The standard care of the unconscious patient was undertaken; several patients also received additional forms of treatment, as shown in Table Vla.

TABLE Vla Additional Forms of Treatment

Treatment	No. of Patients	
	In trial	Excluded from trial
Endotracheal intubation	46	8
Gastric aspiration and lavage	72	12
Assisted respiration	4	3
Bronchoscopy	1	6
Tracheostomy	-	2
Peritoneal dialysis	15	6

Results

33 patients were excluded for the following reasons:

Infection present on admission 20

Aspiration evident on admission 6

Treated elsewhere prior to admission 8

Other 1

A few patients were excluded for more than one reason.

Of 144 patients admitted to the trial, respiratory infections developed in only 8. There were 3 cases among the 73 "treated" patients receiving prophylactic penicillin, and 5 cases among the 71 controls. On the other hand, 18 of the 33 patients excluded from the trial became infected. The types of infection are shown in Table V11.

TABLE V11 - Types of Infection

Type	No. of patients with respiratory infection	
	In trial (144)	Excluded from trial (33)
Bronchopneumonia	2	3
Lobar pneumonia	3	4
Early inflammatory change	2	3
Segmental collapse following aspiration	1	7
Lung abscess	-	1
Total	8	18

Some details of the 8 patients in the trial with respiratory infections are given in Table Vlll. Six of them were undergoing peritoneal dialysis which interfered with physiotherapy, and 6 of them were unconscious for more than 24 hours. It will be seen from Table lX that only 17% of all patients in the trial were unconscious for so long.

TABLE VIII - Patients in Trial Developing Respiratory Infection

Age	Sex	Prophylactic penicillin	Time unconscious after admission (Hrs.)	Clinical details
44	M	Yes	90	Crepitations right base. Temperature 101°F. X-ray; inflammatory changes right base.
60	F	Yes	32	Dull at left apex with crepitations over whole of left chest. Temperature 101°F. X-ray; old tuberculosis cavitation. Bronchopneumonia. Peritoneal dialysis.
52	F	Yes	51	Died of hypotension. No infection clinically. X-ray: partial collapse left base. Peritoneal dialysis.
44	F	No	175	Consolidation right base. Temperature 102°F. X-ray: right basal pneumonia. Peritoneal dialysis.
19	F	No	56	Minimal diffuse signs in chest. Temperature 103°F. X-ray normal. Aspirated after gastric lavage. Peritoneal dialysis.
58	F	No	72	Consolidation right base. Temperature 102°F. X-ray; consolidation right base. Peritoneal dialysis. Bronchoscopy
31	F	No	36	Scattered crepitations right base. Temperature 99°F. X-ray patchy inflammatory changes right base. Peritoneal dialysis. Assisted respiration.
55	M	No	24	No clinical signs. Temperature 98.4°F. X-ray: left lower lobe consolidation.

TABLE IX Period of Unconsciousness

Period	No. of Patients	
	In trial	Excluded from trial
4 hr.	9 (6%)	1(3%)
4-12 hr.	56 (39%)	7(21%)
12-24 hr.	53 (37%)	7(21%)
1 day	8 (5%)	6(18%)
2 days	10 (7%)	5(15%)
Over 2 days	8 (5%)	7(21%)

Period of unconsciousness is measured from time of admission since the exact time the patient became unconscious was usually unknown. This latter period was only rarely more than 8 hours.

Three out of 177 patients died. Two patients died as a result of intractable hypotension, but infection played no part in their deaths. The other patient, aged 84, suffering from coal-gas poison-:ing, was excluded from the trial as she was thought to be infected on admission. She regained consciousness and remained reasonably well for a few days but thereafter lost ground and died of broncho-:pneumonia.

Conclusions

It is often said that the unconscious poisoned patient is par-:ticularly liable to respiratory infection, and that penicillin should be employed as a prophylactic measure in these patients. There is little evidence to support these statements; moreover, the dangers of prophylactic penicillin in other unconscious states have been clearly demonstrated. This study was designed to deter-:mine the incidences of chest infection in a series of unconscious

patients and to attempt to evaluate the role of penicillin in preventing such infection. We found that 26 (15%) of 177 consecutive unconscious poisoned patients became infected, but of 144 patients admitted to the trial only 8 (5.5%) became infected. Three of these had had prophylactic penicillin and 5 had not. In contrast to this low rate of infection in patients accepted for the trial, an infection-rate of 54% was found in the 33 patients excluded from the trial, of whom 32 were either infected when they reached hospital, or were likely to become infected because of aspiration of vomitus or injudicious gastric lavage.

In view of these widely differing infection-rates we suggest that the unconscious poisoned patient on admission, should be designated "clean" or "unclean"; clean patients are those with no evidence of infection, unclean patients are already infected or have aspirated. In practice the distinction between these two groups of patients is not difficult. Thus the 144 patients admitted to the trial were considered "clean" and even in the 8 who became infected there was some factor contributing to the development of infection; for example, in one patient the infection was partly attributable to the aspiration of vomitus during gastric lavage (without a cuffed endotracheal tube in situ). Furthermore in 6 of these patients peritoneal dialysis was performed; this procedure required complete immobilisation and prevented adequate physiotherapy to the chest. We have since modified our management so that intensive physiotherapy can be given to patients undergoing dialysis. Only 1 of the 8 patients in the trial who became infected

was unconscious less than 24 hours. The other 7 were unconscious for longer periods giving an infection-rate of 27% in patients in the trial unconscious for more than 24 hours. But, as other fac-:tors were involved in 6 of these patients - e.g., peritoneal dialy-:sis - we have no evidence at present that prolonged unconsciousness predisposes to respiratory infection. Only 2 of these 8 patients had chest infections of any severity, whereas many of the "unclean" patients excluded from the trial became severely infected.

We have been unable to show any significant difference in the infection-rate between patients receiving prophylactic penicillin and those not so treated. Since other workers have demonstrated the harmful effects of antibiotic prophylaxis, we consider that the use of penicillin prophylactically should be abandoned in the "clean" unconscious patient.

Circulatory Failure

As in so many other forms of shock the exact mechanism which produces it in acute poisoning is not clearly established. Certain hypotheses have been put forward by Shubin and Weil (1965) but are not entirely acceptable. We are currently studying blood volume in shock in an endeavour to explain certain of the changes in the circulation associated with acute poisoning.

"Shock" is on occasions difficult to assess in poisoned patients; it is, however, frequently present. We have selected levels of less than 90 mm. Hg. systolic pressure in a patient over 50 years of age and less than 80 mm. Hg. in younger patients, as indicating shock.

Although the levels selected may seem rather low they have been evolved from experience in treating patients poisoned with sedative drugs. Hypotension might lead to acute renal tubular necrosis or cerebral ischemia or thrombosis. Renal damage was very infrequent and only occurred when the blood pressure could not be kept above these levels for a considerable length of time. There was no ob-:vious mental impairment in the patients after recovery from poison-:ing, but this was very difficult to assess retrospectively as many of the patients already had an underlying mental disturbance. Fine psychological testing was not done.

Metaraminol was the first method used if the blood pressure did not rise satisfactorily when the foot of the bed was elevated. Clemmesen and Nilsson (1961) recommended the use of plasma expanders rather than vasopressor agents and Shubin and Weil (1965) have pro-:duced further evidence to support this. The main risk with vasopressor drugs is excessive constriction of the renal arterioles which may lead to acute tubular necrosis. Metaraminol was used only in small doses so that the systolic blood pressure did not rise above 100 mm. Hg. The finding that urinary flow increased under these conditions (Weil, 1957; Haugen and Roden, 1959) and the low incidence of acute renal failure indicates that in small doses metaraminol is safe and effective.

If two or three injections of 2.5 - 5.0 mg. metaraminol fail, then infusion of low molecular weight dextran, plasma, or even blood should be given. Acidosis frequently accompanies severe shock and will require energetic correction with infusions of 120m. Equiv. sodium bicarbonate. Digitalis and propanalol to correct

arrhythmias may be required. Hydrocortison, 100 mg. six hourly may also be given in severe shock.

Hypothermia

Treatment of hypothermia remains controversial. Some authors have suggested that rapid re-establishment of normal body tempera-:ture is desirable (Burton and Edholm 1955; Lee and Ames, 1965). However, Adolph (1950) showed that warming the skin inhibits endo-:genous heat production in hypothermic subjects. The danger of causing severe and irreversible peripheral vascular failure was suggested by Grant and McMichael (1942) and convincingly established by Duguid, Simpson and Stowers (1961). It seems, therefore, that the aim of treatment should be to prevent further heat loss from the body by providing an environment where the body temperature may be re-established slowly.

Fluid Balance

If the patient is to be treated by conservative measures alone, then it is unnecessary to pass a catheter. Intravenous fluids to maintain hydration, i.e. 1500 ml per 24 hours will be required. This should be given in the form of 1000 ml 5% dextrose alternating with 500 ml of normal saline. If there is any evidence of dehydra-:tion amounts greater than 1500 ml will be required. Appropriate therapy to control electrolyte imbalance may be required.

General Nursing

The general care of the unconscious patient is the same as that for patients unconscious due to any other cause. The patient must be frequently turned with particular attention to the skin. Regu-:lar recording of temperature, pulse and respiration together with level of consciousness must be done. The blisters already described,

should be treated as for burns.

Convulsions

In children convulsions occur more frequently than in adults. The immediate treatment, as has already been stressed in all the headings already mentioned, is that of the convulsion and not of the poison which brought it about. Paraldehyde, intramuscularly or intravenously is usually the most effective drug.

Having dealt with the general principles of basic supportive therapy, attention is now directed to the important aspects of the treatment of poisoning by particular drugs. Just over 50% of the patients admitted over the two years under review - 776 out of 1,524 were suffering from acute barbiturate poisoning. The important features in the management of acute barbiturate poisoning, other than those already referred to under Basic Supportive Therapy, will now be discussed.

CHAPTER 8

ACUTE BARBITURATE POISONING

Historical

Since the 1930's treatment of barbiturate poisoning has greatly changed. Until 1950 therapy consisted of energetic gastric lavage and intensive analeptic drug administration (Koppanyi and Fazekas, 1950). Analeptic therapy enjoyed a further vogue when Shaw (1955) introduced bemegride (Megimide) as a specific antidote to barbiturate but despite its use the mortality rate remained around 20 per cent (Clemmesen and Nilsson, 1961). These disappointing results were attributed to the complications of analeptic therapy (Eckenhoff and Dam, 1956; Myschetzky, 1961; Montani and Perret, 1963). The major complications are cardiac arrhythmias (Jones, Dooley and Murphy, 1950; Kirkegaard and Norregaard, 1951; Reed, Driggs and Foote, 1952) and convulsions which may produce cerebral depression (Riishede, 1950; Roche, Wynne and Haskins, 1950) or irreversible brain damage (Meyer, 1952; Conferences on Therapy, Treatment of the Patient in Coma, 1953). Visual hallucinations and psychoses have also been reported after bemegride (Myschetzky, 1961). The clini-:cal response to these drugs was, moreover, only transient and they were generally ineffective in severe poisoning (Montani and Perret, 1963). For these reasons analeptic therapy lost favour. Also gastric lavage using large quantities of fluid was associated with high incidence of respiratory and circulatory complications. This procedure, therefore, came to be used much less frequently.

Effective supportive therapy, based on work by Kirkegaard (1949)

and Nilsson (1951) was developed in Copenhagen by Clemmesen and Nilsson (1961). This has come to be called the "Scandinavian Method". Although at first severely criticized as therapeutic nihilism (Koppanyi and Fazekas, 1950) it has since been generally accepted as the basic management of acute poisoning (Wynne, 1960, Ohlsson and Fristedt, 1962; Myschetzky and Lassen, 1963a; Montani and Perret, 1963; Linton, Luke Speirs and Kennedy, 1964; Clifton Mackey and McLeod, 1965; Maher and Schreiner, 1965). The main principles are the prevention and treatment of circulatory and res-:piratory failure and the maintenance of fluid and electrolyte balance. Gastric aspiration alone was given. Using this regime Clemmesen reduced the mortality in acute barbiturate poisoning from 20 per cent to 1 - 2 per cent.

Since haemodialysis was first used in the treatment of poison-:ing by Doolan, Walsh, Kyle and Wishinsky (1951) a variety of tech-:niques have been developed which are designed to remove barbiturates from the patient. Other workers have advocated haemodialysis (Bermen, Jeghers, Schreiner and Pallotta, 1956; Lubash, Ferrari, Scherr and Rubin, 1962; Del Greco, Arieff and Simon, 1962; Maher and Schreiner, 1965), peritoneal dialysis (Burns, Henderson, Hager and Merrill, 1962; Berman and Vogelsand, 1964), forced osmotic diuresis (Lassen, 1960; Mychetzky and Lassen, 1963a), and combina-:tions of these (Linton, Luke Speirs and Kennedy, 1964). Exchange transfusion in infants was described by Farquhar (1965) and Cordone and Marchi (1965) and passage of patient's blood over charcoal by Yatzidis (1965). It has been stressed that these measures are not substitutes for good supportive therapy, but may be used in addition

to the basic regime. These procedures are claimed to shorten the period of unconsciousness and reduce the mortality in seriously ill patients.

There has been a recent trend to use these active forms of treatment in an increasing proportion of cases. Lee and Ames (1965) describing a combined therapy of forced diuresis and haemodialysis, suggested that methods to increase removal of the poison should be used immediately in all patients who are "drowsy on admission". Graham (1966) writing in Price's Textbook of Medicine supported this view. Maclean (1965) advocated that in "all but the mildest cases every effort should be made to promote renal excretion of barbitu-:rates "by forced diuresis and diuretics". It appeared to us that the pendulum was again swinging in the direction of unnecessary and perhaps dangerous treatment. It was considered that a review of our experience over the past two years might help to determine the place of these more active measures in the treatment of acute barbiturate poisoning.

Methods

The 776 patients admitted during 1964 and 1965 and who had taken barbiturates were reviewed. A number of these patients had taken a mixture of drugs but in all of the 776 patients barbiturate was the significant poison.

A complete but rapid physical examination was carried out on each patient to assess the severity of the poisoning and to detect organic disease which might influence the management. Pulse, temperature and blood pressure were recorded in every case. Patients were graded according to conscious level.

Grade 1 Drowsy but response to verbal commands.

Grade 2 Response to mild painful stimulation.

Grade 3 Minimum response to maximum painful stimulation.

Grade 4 No response to maximum painful stimulation.

Rubbing the patient's sternum with the knuckles was used as the standard painful stimulus. It was found that the size and activity of the pupils and the state of the limb reflexes were too variable to be useful indices of the severity of the poisoning. Respiratory function was assessed as already indicated by measurement of the minute volume with a Wright's Spirometer. Serum barbiturate levels were estimated by the ultra-violet spectrophotometric method of Broughton (1956) after initial extraction of the barbiturate with chloroform. The type of barbiturate was identified by thin layer chromatography.

Each patient was assessed individually. Active measures for increasing removal of the drug were considered only when the conscious level was grade 3 or 4 and there was persistent respiratory or circulatory failure, or if reduction of the period of unconsciousness was felt to be important because of a pre-existing physical condition such as severe bronchitis and emphysema, hepatic or renal failure. Serum barbiturate levels were not used as criteria for diuresis or dialysis.

Active Therapy to Remove Barbiturate

Peritoneal dialysis by a method based on that of Maxwell, Rockney, Kleeman and Twiss (1959) was used in most patients requiring additional treatment. The few patients in whom there were contraindications to peritoneal dialysis were treated with forced

alkaline mannitol diuresis by a method similar to that described by Linton, Luke, Speirs and Kennedy (1964).

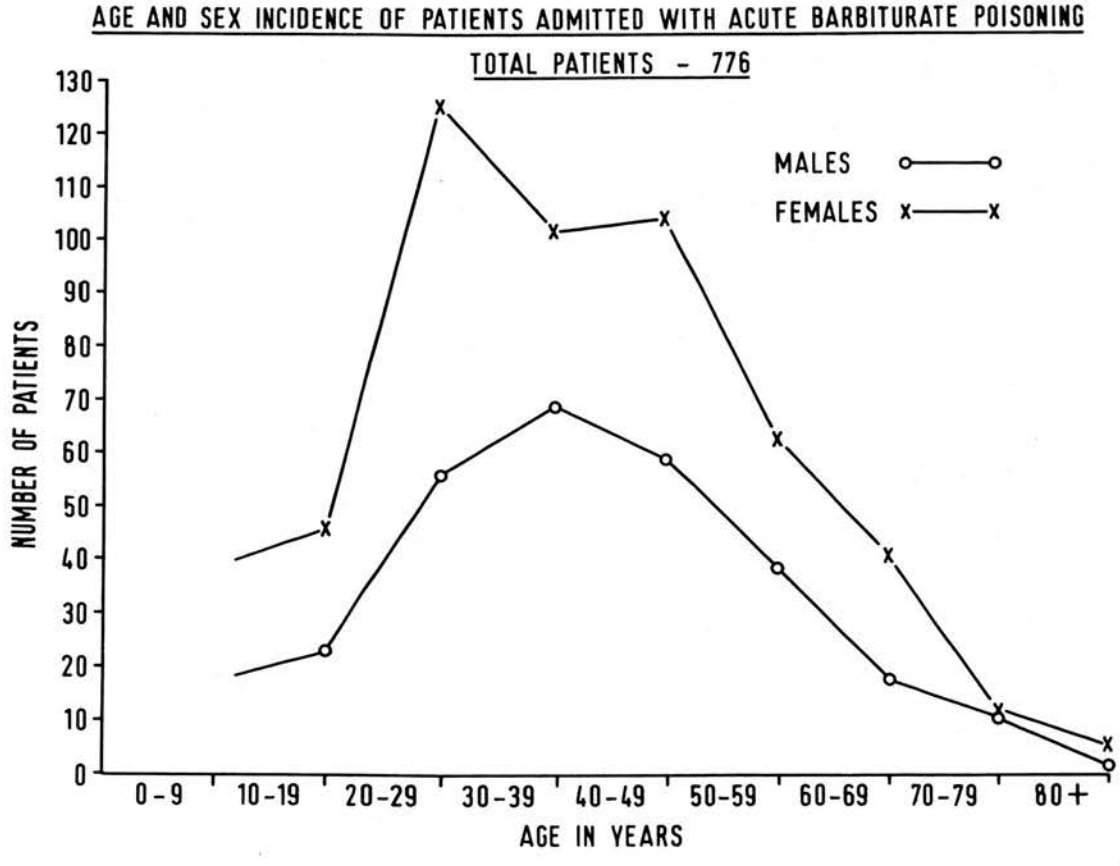
Patients

776 patients (277 males and 499 females) were suffering from acute barbiturate poisoning. 736 (94.8 per cent) of these were treated successfully by basic measures alone. Only 40 (5.2 per cent) had additional therapy to remove the poison. The average length of stay in the Poisoning Treatment Centre was only 2.8 days, although all patients had psychiatric assessment before discharge.

Age and Sex

Figure 8 shows that barbiturate poisoning was commonest in both sexes before the age of 50. There was a high incidence in women under 30 years of age. The poisoning was commoner in females than males and the difference was most marked in the younger age groups.

FIGURE 8



Conscious Levels

The conscious levels were as follows: 193 patients (24.9 per cent) were grade 1 when admitted to hospital. The remaining 583 patients (75.1 per cent) were deeply unconscious. 68 patients, 8.7 per cent of the total, were classified as grade 4.

Serum Levels

The serum barbiturate level was not measured in 268 patients as their clinical condition was entirely satisfactory. The results of the estimation which were made are given in Tables X and XI.

TABLE X Serum Level of Medium and Short-Acting Barbiturate

Serum Barbiturate	< 3.5 mg. per 100 ml.	3.6 - 4.5 mg. per 100 ml.	4.6 - 5.5 mg. per 100 ml.	> 5.6 mg. per 100 ml.
Males	137	17	9	6
Females	218	20	21	8
Total	355	37	30	14
No. Treated by Active Therapy	13	5	9	7

TABLE XI Serum Level of Long-Acting Barbiturates

Serum Barbiturate	<5.0 mg. per 100 ml.	5.1 - 7.5 mg. per 100 ml.	7.6 - 10.0 mg. per 100 ml.	> 10.0 mg. per 100 ml.
Males	33	3	2	-
Females	26	3	3	2
Total	59	6	5	2
No. Treated By Active Therapy	0	1	3	2

Serum levels over 10.0 mg. per 100 ml. for long acting and 3.5 mg. per 100 ml. for short and medium acting barbiturates have been described as "potentially lethal levels" (Berman, Jeghers, Schreiner and Pallotta, 1956). The levels in 83 patients were higher than these figures but only 27 of them were treated by active measures. The remaining 56 patients were satisfactorily managed with basic supportive therapy alone. Two patients in this group with levels of 8.6 mg. per 100 ml. were only slightly drowsy. 13 other patients were given active therapy on account of the severity of their clinical state, but the serum barbiturate levels were below 3.5 mg. per 100 ml.

Complications

Complications present at any time during the poisoning and not necessarily on admission to hospital were studied. The XII shows that 66 patients (8.5 per cent) had serious hypotension. Acute respiratory complications occurred in 38 patients (4.9 per cent), 3 of whom had pre-existing chronic bronchitis. These included infection, atelectasis and central respiratory depression. Hypo-:thermia was present in 137 patients (17.7 per cent) but only 3 had temperatures below 90.0°F. This was most frequent when the patient had been unconscious for some time before admission to hospital. Acute renal failure developed in only 4 patients (0.5 per cent) all of whom had severe persistent hypotension despite treatment. The 4 patients (0.5 per cent) who had cardiac arrest were all very severely poisoned. One of these patients also had acute renal failure.

TABLE XII Complications Associated With the Poisoning

	HYPOTENSION 90mm.Hg.(50 yrs.old) 80mm.Hg.(50 yrs.old)	RESPIRATORY COMPLICATIONS			HYPOTHERMIA		RENAL FAILURE		CARDIAC ARREST
		Chronic	Acute	Acute on Chronic	80.0-89.9 °F	90.0-96.0 °F	Acute	Chronic	
Males	20	9	19	2	1	42	-	1	-
Females	46	3	16	1	2	92	4	2	4
Total	66	12	35	3	3	134	4	3	4

All patients were treated by the basic supportive therapy already described. Gastric aspiration and lavage was carried out in 450 patients (57.9 per cent) using the criteria and precautions stressed previously and there were no complications of note. Of the 66 patients with significant hypotension 51 required intra-:muscular metaraminol. 5 patients required additional treatment with plasma expanders or whole blood. In the remainder the blood pressure was satisfactorily maintained by raising the foot of the bed.

Table XIII shows that 85.0 per cent of patients maintained ade-:quate respiration with an oropharyngeal airway. 16 (2.1 per cent) needed mechanical assisted respiration and only 4 (0.5 per cent) required tracheostomy.

TABLE XIII Methods Used to Maintain Respiration

	Airway Maintained with or without Oro-Pharyngeal Tube	Endotracheal Tube	Mechanical Respirator	Tracheostomy
Males	231	40	4	2
Females	428	57	12	2
Total	659	97	16	4

Acute renal failure was treated by conventional methods. In 2 patients it was transient and haemodialysis was not required. The other 2 were very seriously poisoned. One (Table XV patient 3) who had several complications became uraemic despite peritoneal dialysis and died 48 hours after admission. The other (Table XV patient 4) had a severe brain stem lesion and haemodialysis was not performed. Of the 4 patients who had a cardiac arrest, one responded to external cardiac massage and made a satisfactory recovery while the other three died. Additional active measures to remove barbiturates (Table XIV) were used in only 40 patients (5.2 per cent). Peritoneal dialysis was used in 36 patients (4.7 per cent) and only 4 (0.5 per cent) had forced alkaline osmotic diuresis.

Although an artificial kidney was available, it was not found necessary to use it during the period of this study.

TABLE XIV Additional Methods to Remove the Barbiturate

	Peritoneal Dialysis	Forced Alkaline Osmotic Diuresis
Males	16	3
Females	20	1
Total	36	4

Basic Supportive Therapy

The basic supportive therapy described here was developed from the "Scandinavian Method" (Clemmesen and Nilsson, 1961) but differs from it in several important respects. Oxygen was given by poly-:mask or Edinburgh mask rather than by nasal or oral catheter. We have defined precise criteria for the use of assisted respiration. Although a minute volume of less than 4 litres is an arbitrary index of respiratory insufficiency it has been found to be satisfactory in practice. This has been confirmed by blood gas analyses. An endotracheal tube was never used for more than 36 hours whereas Clemmesen and Nilsson (1961) suggested a limit of 4 days. We have found a high incidence of severe necrotising tracheitis when the tube was not removed after 36 hours. As already mentioned routine pro-:phylactic antibiotics were not given. There was a low incidence of respiratory infection although gastric aspiration and lavage was carried out in nearly 60 per cent of the patients. This is another important difference between our regime and the "Scandinavian Method". Clemmesen and Nilsson (1961) abandoned gastric lavage on the evidence of Harstad, Moller and Simesen (1942). We used gastric aspiration and lavage only when it was known that the drug had been taken within four hours. The importance of this time interval has al-:ready been demonstrated.

Shock was dealt with as detailed under basic therapy and only five of our patients required plasma expanders or hydrocortisone. All four patients who died despite treatment has severe resistant hypotension. Severe acidosis was uncommon in our series but should

always be looked for and treated in unresponsive shock.

Bemegride

For reasons already mentioned we agree with Clemmesen and Nilsson (1961) and Myschetzky (1961) that bemegride should not be used. For severe respiratory depression a single injection of nikethamide (Coramine) may be given as a respiratory stimulant while other supportive measures are being prepared.

Serum Barbiturate Level

Serum barbiturate level was not regarded as an important indication of the severity of poisoning. The lack of consistency in response of experimental animals and even more of humans, to hypnotic drugs is one of the most complicating and disturbing factors in critical studies of poisoning. The general problem of variation in response to drugs has been reviewed by Richards and Taylor (1956), who showed that the response to barbiturates in experimental animals could vary by as much as 50.0 per cent. They also showed that an animal could respond to the same dose in different ways on repeated occasions. These findings show the difficulty in selecting satisfactory control groups. Even individual subjects of studies cannot be their own controls. The possibility of acquired tolerance to hypnotic drugs is a further consideration. There are many studies both on animals (Kinsey, 1940a, 1940b, 1940c; Gruber and Keyser, 1946), and on humans (Isbell, Altschul, Korntsky, Eisenman, Flanary and Fraser, 1950; Brodie, Mark, Lief, Bernstein and Papper, 1951) which confirm the development of tolerance to barbiturates.

In the present study the serum barbiturate levels frequently

were not closely related to the clinical state. More than half of the patients with "potentially fatal levels" (Berman, Jeghers, Schreiner and Pallotta, 1956) did not require, by our criteria, peritoneal dialysis or forced alkaline osmotic diuresis and recovered satisfactorily with supportive therapy alone. However, 13 patients with levels in the suggested safe range did require active therapy. The measurement of serum barbiturate may often be of diagnostic value but is not essential for assessing the severity of the poisoning. This is particularly so in epileptic patients and others habituated to these drugs. Two patients had serum levels of medium acting barbiturate of 8.6 mg. per 100 ml. and were only slightly drowsy. Both patients regularly took barbiturates for night sedation and had become habituated to the drug. They were each treated satis-:factorily with basic supportive therapy. In our experience the use of serum barbiturate levels as strict criteria for the use of active measures for removal of the poison as suggested by Lee and Ames (1965) does not seem justified. In assessing a patient with barbiturate poisoning the serum level should always be considered in relation to the patient's history and clinical condition and should never take precedence over the latter (Maher and Schreiner, 1965).

Enhanced Removal

The use of methods to increase removal of the poison is a logi-:cal approach to the treatment of severe acute poisoning. Several workers (Lassen, 1960; Ohlsson and Fristedt, 1962) have suggested that the period of unconsciousness is reduced by these measures and Myschetzky and Lassen (1963a and 1963b) have gone so far as to claim

that the period of unconsciousness may be reduced to as little as one third of that achieved with supportive therapy. This was assessed by comparing 57 patients treated by forced diuresis with 82 others who were not. For the reasons stated above this is not a satisfactory control group. Other authorities have assessed these additional measures by the increase in elimination rate of barbiturate. The standard method of estimation of barbiturate was that of Broughton (1956) which measures non-toxic metabolites as well as the active drug (Maynert, 1952; Bloomer, 1965). As these metabolites are water-soluble and therefore readily dialysable an apparent increase in removal rate may be misleading (Bunn and Lubash, 1965). Methods of extraction of the barbiturate from test samples prior to application of the Broughton method of measurement vary and therefore different series may not be comparable. Even haemodialysis which is the most efficient method of removing dialysable poisons (Allwall, Lindgren and Lunderquist, 1952; Linton, Luke, Speirs and Kennedy, 1964; Maher and Schreiner, 1965) does not remove large quantities of the drug. In barbiturate poisoning, with the exception of barbitone (Balme, Lloyd-Thomas and Shead, 1962) and phenobarbitone which are more readily dialysable, haemodialysis removes the equivalent of only a few tablets, although the ingested dose may have been very large. Maher and Schreiner (1965) and Lee and Ames (1965) suggested on clinical impression that the small quantity removed may be of considerable pharmacological and clinical significance. This is also our own impression but there is no objective evidence to substantiate it.

In the present state of knowledge there is no objective method of measuring a patient's progress towards recovery of consciousness. Also there is no means of predicting how long he will remain unconscious. Evaluation of these methods of increasing removal of toxic substances from the body, therefore, depends largely on clinical impression which is notoriously unreliable. All these therapeutic procedures are, except in experienced hands, likely to result in severe complications, such as upsets of fluid and electrolyte balance. It would seem unwise, therefore to initiate these procedures without extremely careful assessment. The suggestion that all patients who are merely drowsy should be treated by forced diuresis, Lee and Ames (1965), Maclean (1965), Graham (1966) is unjustifiable. The results presented in this series where 95 per cent of patients were treated successfully by supportive therapy alone favour the view that active methods to increase removal of the drug should be reserved for a very small proportion of severely poisoned patients.

Mortality

In the two years of this review the mortality rate for the total of 1,524 patients suffering from acute poisoning was 1.4 per cent. Of the 776 patients with acute barbiturate poisoning only 6 died (0.8 per cent). The clinical details of these 6 patients are given in Table XV. All of these patients were seriously poisoned. 2 of them (patient 1 and 2) died within a few minutes of admission to hospital before active therapy could be started. The other 4 patients who died all had maximum therapy and showed improvement as judged by a rise in conscious level and a fall in serum barbiturate level. Post mortem examination showed an astrocytoma and acute

pancreatitis in patient 3 and patchy cerebral necrosis in patient 4. Patient 5 died in irreversible shock and extensive pulmonary infarc-:tion was found in patient 6.

TABLE XV Details of the 6 Patients Who Died

Patient	Age	Drug(s) Taken	Serum Level	Clinical Features
1.	60	Cyclobarbitone	8.6 mg. per 100 ml.	Conscious level grade 4. Cyanosed. Systolic blood pressure 70 mm. Hg. Cardiac arrest. Died a few minutes after reaching ward. Post Mortem showed inhalation of vomit with fulminating bronchopneumonia, healed myocardial infarct, multiple small cerebral and pontine infarcts.
2.	23	a) Phenobarbi-:tone b) Codeine compound tablets	Serum barbiturate 1.6 mg. per 100 ml. Serum sali-:cylate .36mg. per 100 ml.	20 weeks pregnant. Conscious level grade 4. Markedly cyanosed. Stertorous respiration. Endotracheal intu-:bation. Systolic blood pressure 104 mm. Hg. Methaemo-:globin level of 4.0 G. per 100 ml. Cardiac arrest and death a few minutes after admission. Post Mortem confirmed barbiturate and salicylate poison-:ing but showed no other abnormality.
3.	57	a) Butobarbitone b) Small quantity of Cyclo-:barbitone c) Numerous herbal mixtures	4.8 mg. per 100 ml.	Unconscious for 24 to 48 hours before reaching hospital. Conscious level grade 4. Blood pressure unrecordable. Rectal temperature 88°F. Hyperventilation, respiratory rate 28 per minute. Endotracheal intubation. Peritoneal dialysis. Serum barbiturate level fell to 1.9 mg. per 100 ml. Conscious level rose to grade 2. Hypotension difficult to control. Developed flaccid paralysis of all limbs and acute renal failure. Died 48 hours after admis-:sion. Post mortem showed an astrocytoma of the occipital lobe, tracheobronchitis and acute pancreatitis.

TABLE XV (contd.)

Patient	Age	Drug(s) Taken	Serum Level	Clinical Features
4.	50	Sodium Amylo-:barbitone.	1.9 mg. per 100 ml.	Conscious level grade 4. Severely hypotensive. Respira-:tion depressed. Endotracheal intubation. Peritoneal dialysis not given because of old tuberculosis peritoni-:tis. Forced alkaline osmotic diuresis. Conscious level and general condition improved considerably over 24 hours. Later developed acute renal failure and clear signs of a brain stem lesion. Not haemodialysed. Died 13 days after admission. Post Mortem showed patchy cerebral necrosis, broncho-pneumonia of right lung and acute pyelonephritis of left kidney.
5.	69	Sodium Amylo-:barbitone	5.7 mg. per 100 ml.	Conscious level grade 4. Blood pressure unrecordable. Marked respiratory depression (minute volume 1.6 litres). Rectal temperature 85°F. Endotracheal intubation. Peri-:toneal dialysis. Respiration improved. Serum barbiturate fell to 1.4 mg. per 100 ml. Hypotension persisted despite maximum therapy. Cardiac arrest. Died 52 hours after ad-:mission. Post Mortem showed only early bronchopneumonia.
6.	54	Phenobarbitone	11.0 mg. per 100 ml.	Known epileptic for many years. Delay of 24 hours before admission. Conscious level grade 4. Markedly cyanosed. Collapse of left lung. Bronchoscopy. Endotracheal intuba-:tion. Peritoneal dialysis. Despite serum barbiturate falling to 4.6 mg. per 100 ml. gradual deterioration. Shocked. Died 44 hours after admission. Post Mortem showed congestive cardiac failure, confluent bronchopneumonia and extensive pulmonary infection. Source of embolus not found.

CHAPTER 9

SALICYLATE POISONING

(a) Frequency

Salicylate either in the form of acetylsalicylic acid or along with phenacetin and codein was the second commonest drug taken. 210 patients out of 1,524 or 13% indulged in this form of poisoning.

(b) Diagnosis

The diagnosis is usually readily made in an adult as the patient unless very seriously poisoned will be conscious. In little children drowsiness, disorientation and unconsciousness may be present. Salicylates, in toxic doses, by increasing the sensitivity of the respiratory centre to CO_2 produce initially a respiratory alkalosis and subsequently because of their acid nature a tendency to metabolic acidosis. In our experience acidosis as indicated by blood pH. is, however, very rare. The predominant effect on the acid balance depends largely on the age of the patient. The younger the sufferer the earlier the appearance of acidosis. Even in adults, acidosis as measured by arterial blood pH. is very uncommon.

(c) Clinical Features

The general metabolic effect results in agitation, tachypnoea, hyperventilation, profuse sweating, tinnitus, deafness, blurring of vision, nausea and vomiting, hyperpyrexia and tachycardia. When the salicylate has been taken in a compound tablet with phenacetin, sulph or methaemoglobinaemia may also be evident. The urine may contain albumin and the Addis count rises markedly due to

desquamation of renal tubular cells. The Phenistix test is posi-:tive the urine giving a purple reaction. Clinically it is very difficult to assess the severity of salicylate poisoning. A serum salicylate level of 50.0 mg. per 100 or more in an adult indicates moderate or severe poisoning. Sudden death may occur for no appa-:rent reason, this is perhaps associated with the rapid hypokalaemia which occurs in association with the metabolic changes. Loss of consciousness or even drowsiness in acute salicylate poisoning is of grave significance, the morality in this group being high.

Treatment

Treatment of moderate or severe salicylate poisoning is a matter of urgency and if suspected on clinical grounds should be initiated straight away pending the results of the serum salicylate level. As already stated it is never too late to undertake gastric aspiration and lavage in salicylate poisoning. In spite of what some authors suggest it is not advisable to leave sodium bicarbonate in the stomach as its presence promotes absorption of any salicylate remaining. Immediately after lavage forced alka-:line diuresis as described by Cumming (1964) is started. The rate of infusion is very important and should be 500 ml. every fifteen minutes for 3 hours. At the end of this time the serum salicylate will have been at least halved and the patient well on the way to recovery. The rate of infusion may then be reduced to 500 ml. per hour and discontinued usually six hours after start-:ing. The fluids infused should be normal physiological saline, 5% laevulose and 1.25% sodium bicarbonate, 500 ml. of each in rotation. The object of the bicarbonate is to alkalinise the

urine and correct any acidosis. This is important as, if the pH of the urine is raised from 6.6 to 7.6 the elimination of the salicylate increases almost tenfold. The patient will be de-:hydrated from overbreathing, sweating and vomiting therefore there is no call for concern if, despite the amount of fluid infused, no urine is passed for the first 90 minutes. Urinary catheterisation is seldom necessary.

As already stated as hypokalaemia may develop rapidly care-:ful control of plasma electrolytes is essential and potassium supplements given as required.

Peritoneal Dialysis and Haemodialysis

If forced diuresis cannot be undertaken owing to the presence of such conditions as myocardial insufficiency or renal impairment, which are rarely present as it is young people who usually take salicylate, peritoneal dialysis or haemodialysis should be given. On very rare occasions the respiratory stimulation may result in such rapid and severe overbreathing that curarization of the patient and mechanical respiration may be necessary. In view of a possible bleeding tendency in this form of poisoning Vitamin K_1 10 - 20 mg. should be given intramuscularly.

In children salicylate poisoning is especially dangerous where despite an apparently safe serum level of 30.0 mg. per 100 ml. the severe acid base disturbance to which children are more susceptible may prove fatal.

Serum Salicylate Levels as found in the 192 patients are seen in Fig. 9.

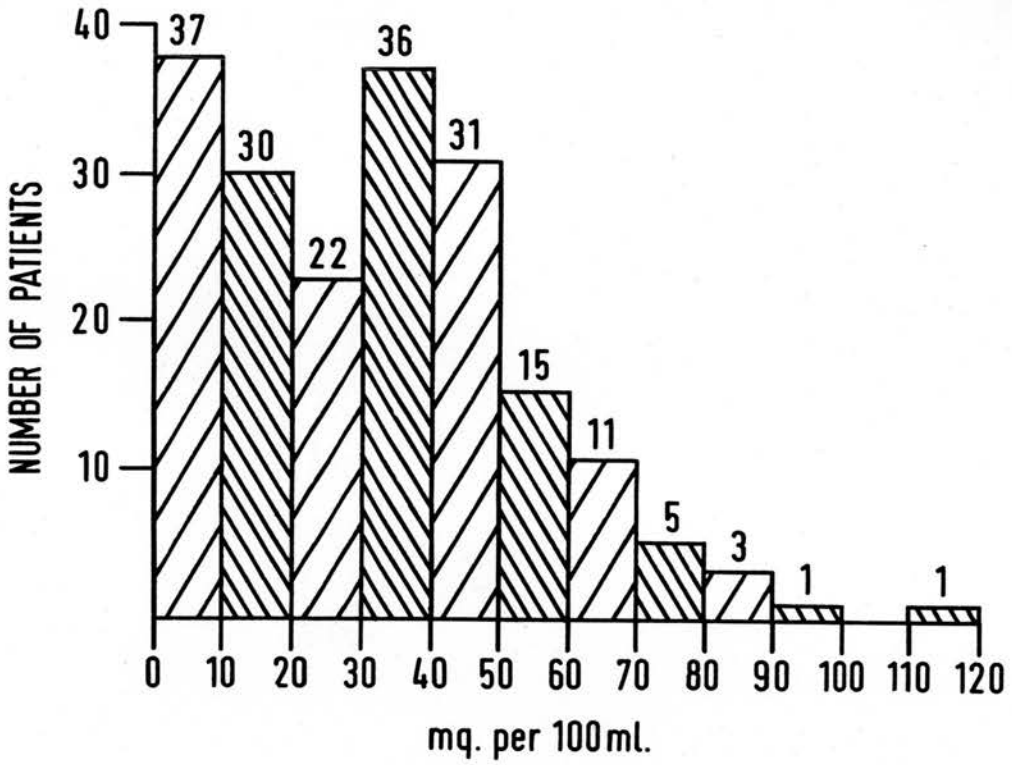


Fig.9. Initial Serum Salicylate Level.

With one exception all those with a level of 50 mg. per 100 ml. or over were treated by the regime of forced alkaline diuresis already described. Eleven with initial levels between 45 and 50 mg. per 100 ml. also had forced alkaline diuresis as, is so often the case, the serum salicylate level rose after gastric lavage. Forty-five patients, therefore, had forced alkaline diuresis undertaken. This therapy achieved a rapid fall in salicylate level, the level usually falling to half the original after four to five hours. This corresponded with marked clinical improvement.

Mortality

There was no fatality and no morbidity, a satisfactory outcome for the mortality from acute salicylate poisoning in adults is usually about 3%. (vq)

Potassium Supplements

Difficulties were encountered as to the precise role of intravenous potassium supplements during the forced diuresis. Serum potassium levels as very dangerously low as 1.9 mg. per 100 ml. were recorded without any apparent deleterious effect. Efforts are currently being made to determine the cause of the fall in serum potassium; alkalosis, gastric aspiration and lavage, and the regime of forced diuresis employing sodium bicarbonate being obvious factors but they do not appear to be the sole causes. Until further information is available our current practice is, as suggested already, to undertake frequent estimations and add potassium to the intravenous regime whenever the serum level drops below 3.0 mg. per 100 ml.

The single patient with a salicylate level over 50 mg. per 100 ml. who had treatment other than the forced alkaline diuretic regime was also the only instance of homicidal poisoning that we recognised. The patient suffered from coronary vascular ischaemia and a minor degree of congestive heart failure in addition to severe osteo-:arthritis. She had been given a large dose of salicylate disguised by her customary nightcap. On admission she showed all the features of moderately severe salicylate poisoning along with congestive heart failure. The serum salicylate level was 69 mg. per 100 ml. She was treated by peritoneal dialysis, the rather low amount of two grams being recovered in the dialysate. This recovery could well have been enhanced by adding albumen to the dialysate. Her congestive heart failure, as would be anticipated, was greatly im-:proved by manipulating the glucose content of the dialysing fluid. Her recovery from the poisoning was uneventful and the poisoner received but a nominal sentence!

Combined with Other Drugs

Many patients had taken their salicylate along with codein and phenacetin but apart from occasionally encountering methaemoglobin-:aemia the main upset was caused by the salicylate overdose. The apparent cyanosis brought about by the presence of the methaemo-:globinaemia in the setting of tachypnoea, tachycardia, pyrexia, sweating and exhaustion can lead the unwary to a diagnosis of res-:piratory infection for which salicylate is then prescribed as part of the symptomatic therapy. This pattern of events can occur especially in children with fatal results.

CHAPTER 10

COAL GAS POISONING

Frequency

The third most common form of poisoning encountered was that from carbon monoxide poisoning. 150 patients were admitted over the two years representing 10% of the total.

Self and Accidental Poisoning

Coal-gas is frequently the choice of the elderly when indulging in self poisoning. As already stressed it is very important to regard all instances of coal gas poisoning in the elderly as self poisoning or suicidal poisoning unless proved otherwise. Too often out of misplaced kindness an episode of self poisoning by coal-gas is dismissed as accidental owing to the sufferer's lack of sense of smell, impaired vision and poor powers of concentration. To designate the act as accidental is frequently to deny the appeal factor which is contained in the manipulative act of self poisoning. Elderly people living on their own frequently are severely depressed or distressed and indulge in self poisoning by coal gas in an attempt to rectify the situation.

Carbon monoxide is toxic in man only in the sense that it combines with haemoglobin 210 times more strongly than oxygen, thereby depriving the tissues of oxygen. There is some evidence that it has a direct toxic effect on certain bacteria and sea urchin's eggs. The effects of the carbon monoxide on humans depends to a large part on the ability of the patient to withstand hypoxia. Thus elderly persons with generalised atherosclerosis are more liable to

be adversely affected because their vital organs are less well able to withstand hypoxia than those of healthy young adults. Children, however, are notoriously susceptible to carbon monoxide due to the smaller amount of haemoglobin available in the child.

The composition of domestic gas varies in its carbon monoxide content in different parts of the country. In Dundee where coal gas poisoning is very uncommon it is but 7%. In Edinburgh it forms 14% of domestic gas. Other parts of the country are supplied by natural gas which is almost pure methane with very little carbon monoxide.

Mortality Carbon monoxide causes by far the greatest number of deaths from poisoning accounting for nearly 70%. The majority of these deaths take place outside hospital since the gas is such a rapid killer. Of 192 deaths from domestic gas poisoning recently investigated as to the locus of the death, 181 died at home and only 11 in hospital (Registrar General for Scotland 1963). Despite this high proportion of deaths at the scene of the poisoning the survivors admitted to hospital still show the highest mortality compared with other poisoning. The hospital mortality from carbon monoxide being around 7%; that from salicylates 3% and barbiturates 2%. This high death rate from carbon monoxide poisoning (6% in our series) even in hospital is largely accounted for by the fact that it is chiefly in elderly atherosclerotic patients that coal gas poisoning is found. These elderly patients seldom die immediately after admission but after pseudo recovery lasting a few days, deterioration occurs and death ensues from the complications of the episode of gassing.

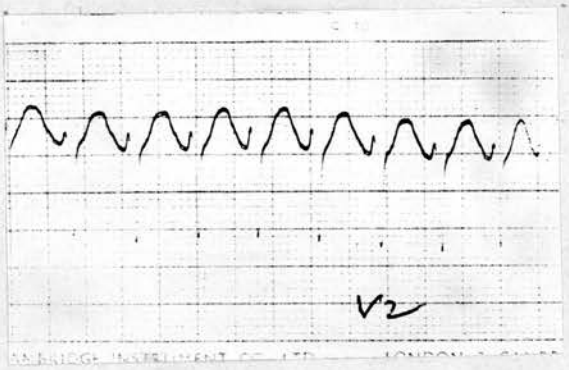
Complications During 1964 particular attention was paid to the complications of carbon monoxide poisoning as this feature of the condition had not previously been studied. Of the 69 patients suffering from this form of poisoning 23 (30%) showed some complication which could be attributed to the gassing. These complications are shown in Table XVI

TABLE XVI Complications of Carbon Monoxide Poisoning

	Mild	Moderate	Severe	Totals for each system
Cardio-vascular	9	4	3	16
Central Nervous	1	1	4	6
Gastro-Intestinal	0	2	2	4
Respiratory	0	1	2	3
Skin Lesions	2	0	1	3
Other	0	0	2	2
T O T A L				34

It is seen that cardio-vascular complications are the most common. That such changes occurred was shown by Klebs in 1865 and Stearns (1938) found 21 out of 22 patients showed electrocardiographic abnormalities.

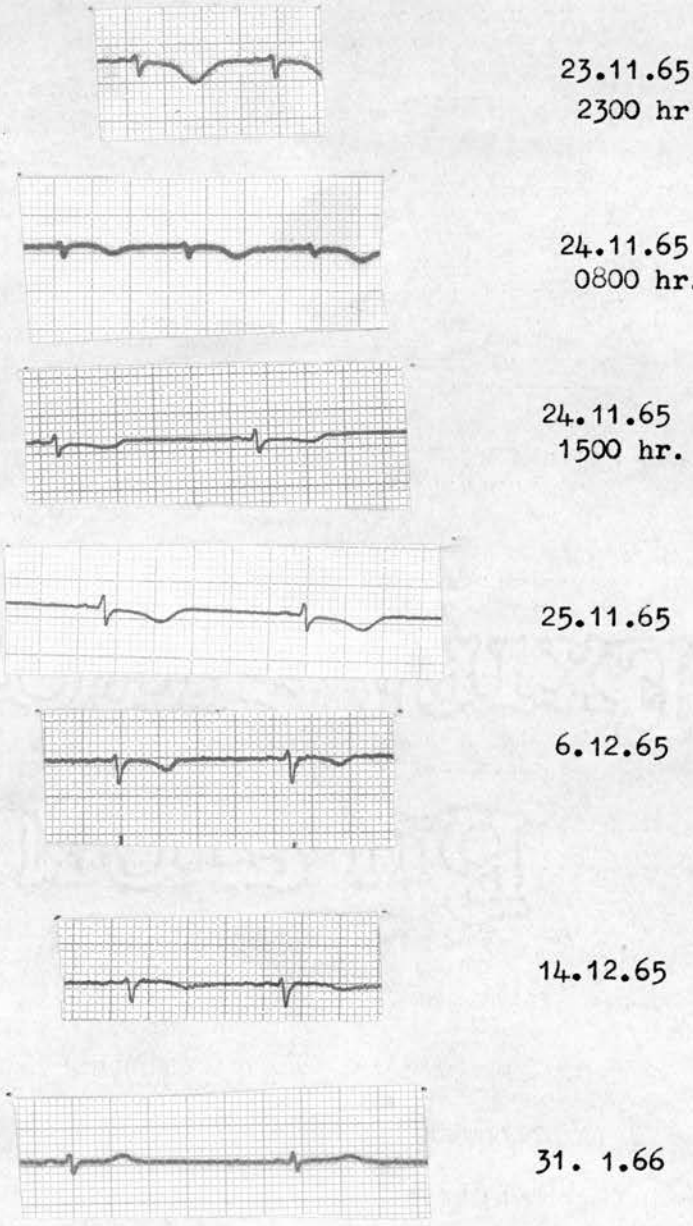
In this series 46% of patients over 65 had recent changes in their electrocardiograms, the record returning to normal a few days later. Fig. 10 shows the change in rhythm brought on by carbon monoxide poisoning and its spontaneous reversion to normal.



A. J. 10.12.65. 3-30 pm.

A.J. 10.12.65. 3-45 pm.

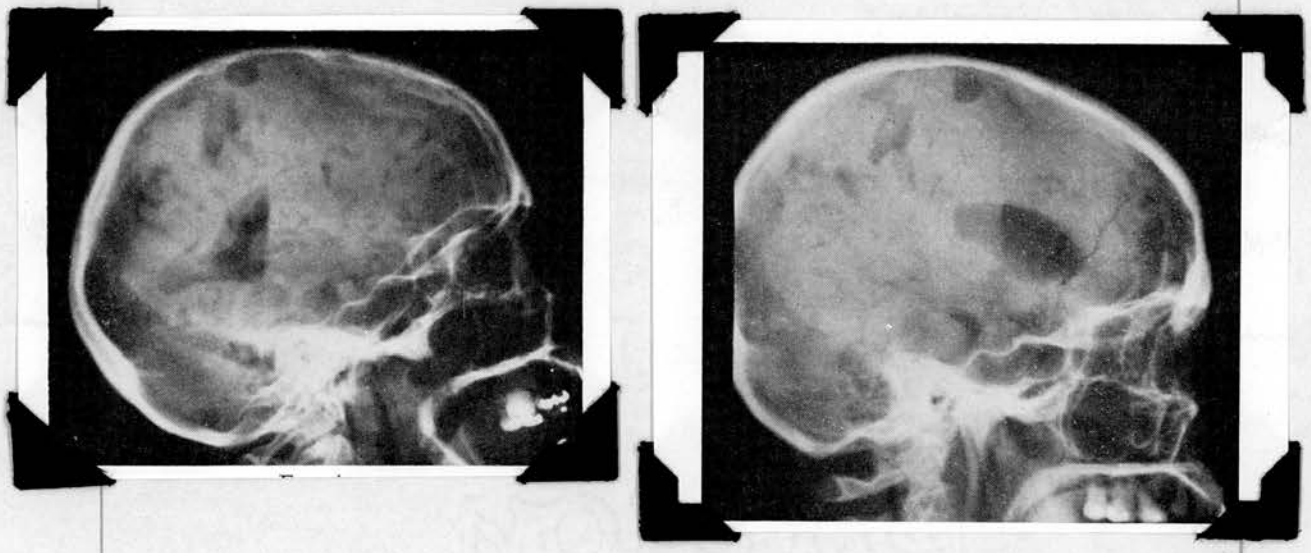
Fig. 11 shows the changes in a 14 year old anaemic girl poisoned by coal gas. Reversion to normal only occurred after several months.



Lead aVl

Central Nervous System

Complications were also encountered in the central nervous system. Owing to lack of sensitive testing it was difficult to assess the frequency. One patient developed akinetic mutism but eventually recovered and was able to resume her domestic duties. Her air encephalogram is shown in Fig. 12.



Recovery from this unusual complication is quite exceptional and the patient concerned probably owes her survival to the devoted nursing care applied over very many weeks.

Haematemesis occurred in four patients.

Pancreatitis, a previously unrecorded complication, has been observed in several patients. This latter finding is being pur-:sued further. Bullous skin lesions, respiratory and renal

complications were observed in a few patients.

Psychiatric conditions relevant to the gassing but believed to have existed before these episodes were found in all but 16 of the 69 patients admitted in 1964. Thus substantiating the plea that such abnormalities must be sought for and the episode not dismissed as "accidental".

Treatment

54 patients out of 69 were considered ill enough to warrant 5% CO_2 and O_2 mixture. In no instance did we observe further depression of the respiratory centre and in several patients stimulation of the respiratory centre was noted. Blood gas analysis was not, however, undertaken to confirm the value of 5% CO_2 + O_2 administration or to confirm or refute that CO_2 retention existed in these poisoned patients.

No hyperbaric oxygen chamber is available in Edinburgh but we do not consider this has prejudiced the chances of recovery of the patients admitted to hospital. In the first stage of carbon monoxide poisoning the feature is a primary anoxic phase, this leads to capillary damage which produces cerebral anoxia which leads to the second stage of further capillary damage with cerebral oedema. Hyperbaric oxygen is of distinct value in the primary phase and there is no substitute, but time is the vital factor. A patient removed into the fresh air and given O_2 + 5% CO_2 to breathe will reduce the carboxyhaemoglobin level from a lethal level of 70% to below 50% in twenty minutes. Thus for hyperbaric oxygen to be of value in this stage the patient would have to be placed in a fully primed chamber within 20 minutes of being found gassed. The average time

between our patients being found gassed and admitted to hospital was 85 minutes. The answer to this problem lies in the provision of portable chambers which can be rushed to the scene of the gassing.

Hypertonic Mannitol

In the second stage of cerebral oedema hyperbaric oxygen is beneficial but it is doubtful if it is of greater value than the infusion of hypertonic mannitol. We are impressed by the efficiency of this therapy, 500 ml. of 20% mannitol being given in 20 minutes followed by 5% dextrose over the next four hours. By this simple and safe measure the papilloedema and venous engorgement so fre-:quently present on admission and presumably denoting cerebral oedema rapidly disappears. Evidence of this dramatic change is currently being recorded with the retinal camera.

Conclusions

Carbon Monoxide kills more people than any other poison in Great Britain. It has its most lethal effects at the extremes of life. The chances of dying of this form of poisoning are much higher than with any other poison and preventive measures have more to offer with this type of poisoning than does treatment. Adequate maintenance of fittings would do much to reduce the number of truly accidental poisonings, but the importance of this form of self poisoning in the elderly is again emphasized.

The carbon monoxide content of domestic gas will be reduced to below lethal proportions in this country in about three years. If the experience in America is followed the number of persons poisoning themselves by this gas will obviously be greatly reduced but the total number of persons committing suicide or self poisoning

will not diminish as other methods take the place of gassing.

CHAPTER 11

RELATIVE FREQUENCY OF DIFFERENT POISONS

Barbiturate, salicylate and carbon monoxide poisoning accounted for 74% of admission. Frequently more than one drug was taken at one and the same time. The highest number in this series was fourteen. A distraught patient emptied the entire contents of the home medicine cupboard down her throat. When more than one drug was taken classi-:fication is under the major drug believed consumed. The remaining groups involved are - other hypnotics 4%, tran-:quillisers 7%, antidepressants 3%. This then leaves a heterogenous mixture of patients amongst whom there are those suffering from overdosage of such drugs as digitalis, quin-:dine, anticoagulants, antibiotics, insulin, iron and household remedies.

CHAPTER 11

NON-BARBITURATE HYPNOTICS

a) Glutethimide

There were 25 instances of acute glutethimide poisoning. It is fortunate that doctors in this country are less susceptible to encouragement and pleas to change from well tried effective hypnotics to the latest "safe new non-barbiturate hypnotic" which the drug houses promote in expensive sales campaigns. Fortunate because, for example, in America, glutethimide is now very widely prescribed and poisoning by this drug is reasonably common. If it were indeed safer and more effective than the barbiturates, then there would be full justification in employing it. Glutethimide is barely soluable in water but very soluble in alcohol. As overdoses of drugs are frequently associated with excessive alcohol intake, the combination of glutethimide and alcohol can be es-:pecially dangerous. It is a difficult poison to deal with and one which gives rise to a variety of clinical features which are more dangerous than those associated with barbiturates. One of the features of glutethimide is that the sufferer is prone when unconscious to sudden attacks of apnoea, in addition there is a direct effect on the myocardium, more severe than that encountered in barbiturate poisoning. The state of consciousness and the findings in the central nervous system fluctuate and this is said to be due to the drug being secreted in the bile and reabsorbed, a process of re-cycling. Attempts have been made to improve the clinical state in severe glutethimide poisoning by draining the

bile duct. Recovery of poison, however, was disappointing. We found that the serum levels of glutethimide that can be regarded as likely to give rise to severe poisoning are above 3.5 mg. per 100 ml. On account of this relatively low concentration the gradient between serum and any dialysing fluid is not of a sufficient order to secure recovery of very significant amounts of the drug in the dialysing fluid. However, as poisoning by this drug has a mortality rate of 60% in patients with levels above 3.5 mg. per 100 ml. either peritoneal or haemodialysis should be undertaken in addition to basic supportive therapy. As the attacks of apnoea have been shown to be preceded by a rise in intracranial pressure intravenous infusion of 500 ml. 20% mannitol over 20 minutes should be administered whenever increased intracranial pressure is suspected.

The 25 instances of glutethimide poisoning fortunately represents a much lower percentage than occurs in most American series. There were no deaths.

Methaqualone

The intensive sales drive for methaqualone only started at the end of 1965, hence only three patients with this form of poisoning are included. As an aside, in the first five months of 1966, 25 patients suffering from overdosage of this drug were admitted indicating just how effective really intensive sales promotion can be.

CHAPTER 13

OTHER ANALGESICS PARACETAMOL (PANADOL)

It is a curious quirk of statistics that Panadol, one of the safest of drugs, has statistically by far the highest mortality in this series. Out of six patients poisoned with this drug two died. Admittedly they were also having, or recently had had, other drugs. However, the evidence, including post mortem histological section, is strongly in favour of paracetamol being responsible for acute liver necrosis from which both patients died. This finding has not previously been recorded with paracetamol overdose but the manufacturers warn that it may happen.

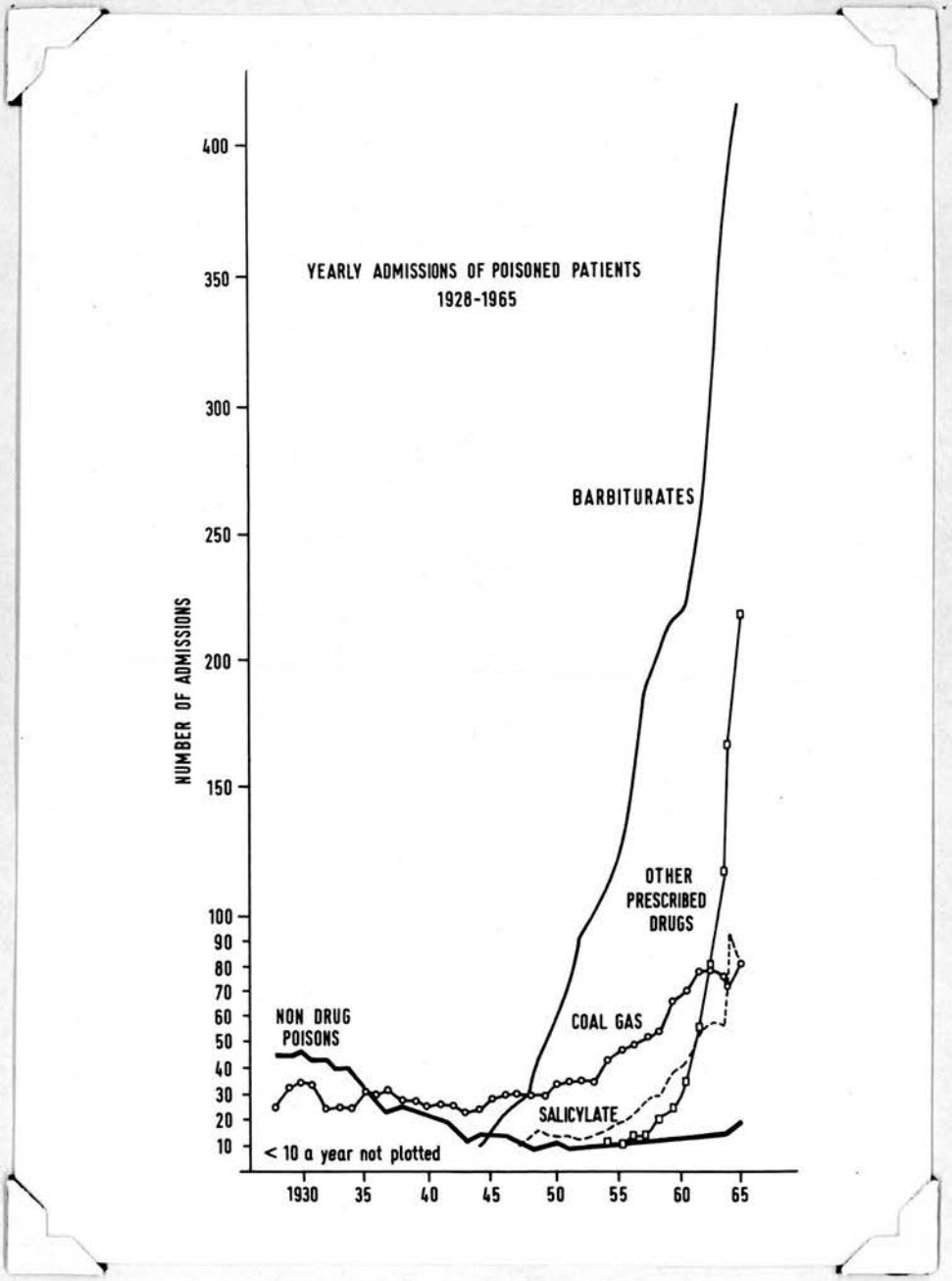
The details of the two fatal cases have been submitted for publication by one of my junior colleagues, hence further descrip-:tion and comment is withheld.

CHAPTER 14

TRANQUILLISERS

Frequency

Poisoning with these drugs is steadily increasing as is shown in Fig. 13.



Clinical Features

The tranquillisers are frequently taken along with barbiturates but the effects even when they are swallowed alone are in no way characteristic. Varying degrees of unconsciousness will be produced with frequently retention of the limb reflexes and dilated pupils beyond what would be expected for a similar degree of unconsciousness due to barbiturate poisoning. Hypothermia is commonly reasonably severe. The blood levels encountered in unconscious patients are in the region of 100 ug.

102 instances of poisoning were encountered. 78 as isolated and 24 associated with other drugs.

Treatment was entirely symptomatic. As would be anticipated due to the poor gradient for dialysis this therapy is of no avail. Forced diuresis may be of some value but as the precise metabolism and detoxication of this group of drugs is not yet known it is uncertain how much of the active principle of the drug will be excreted in the urine.

Mortality

There were no fatalities and no morbidity consequent upon taking this group of drugs.

CHAPTER 15

ANTIDEPRESSANT DRUGS

a) Amphetamine should no longer be prescribed for depression but is included in this section for convenience.

Frequency

In seven instances amphetamine alone had been taken. Combina-:tions of amphetamine and barbiturates were encountered on four occasions; the effect of the barbiturate outweighed that of the amphetamine. On most occasions these drugs had been taken for "kicks" and something had gone wrong usually on account of imbibing alcohol at the same time. One patient had taken a large number of the combined drugs in an act of self poisoning. He had obtained the drug initially to dope his greyhound. His life was saved by his general practitioner giving him artificial respiration during an 18 mile ambulance journey.

Excretion

In poisoning by amphetamine alone excretion will be enhanced by making the urine acid.

b) Mono amine oxidise inhibitors Overdosage with antidepressants of the mono amine oxidise inhibitor group were seldom encountered probably owing to the fact that the "cheese effects" and reactions with other drugs are so well known to psychiatrists and general practitioners in this area that this group is not often prescribed. Only two patients with overdosage of this group were admitted.

c) Amitryptyline, Imipramine, Nortriptyline. These potent anti-:depressant drugs are also becoming more common in self poisoning.

This might be expected for depressed patients are the very people who are likely to indulge in self poisoning.

Clinical Features

The effects are more evident in children in whom a galaxy of arrhythmias are produced in addition to the other features of neuro-:muscular irritability, hypertension, hyperthermia and varying degrees of unconsciousness.

Blood Levels

The levels reached in the blood are low hence once again dia-:lysis is unproductive but forced diuresis may be of value. If serious difficulties in controlling arrhythmias are encountered a cardiac pacemaker may need to be employed temporarily.

Frequency

33 instances of poisoning were treated. No real difficulties were encountered except in one patient in whom the atropine like effects of the drug produced acute retention of urine and paralytic ileus.

CHAPTER 16

MISCELLANEOUS DRUGS

The following drugs are included as although experienced only on a few occasions something of interest or importance arose from each episode of poisoning.

a) Cycloserine Six patients with overdosage of this antibiotic which has a recognised side effect of depression, even when used in small doses for chronic infection, were encountered. One patient, aged 25, who had had a nephrectomy undertaken for hydrone-:phrosis and pyelonephritis and who was on long term cycloserine 0.25 mg. on alternate days took 3 g. in an act of self poisoning.

Clinical Features

On admission she was acutely ill and semi-conscious, was very pale, and appeared to be shocked. There were no laterlizing signs in the central nervous system, no tremor, and no twitching. The tendon reflexes were exaggerated. Apart from her operation scars no other abnormality was detected. Haematological examination, blood urea and electrolytes, chest x-ray films and electrocardiogram findings were all normal. The plasma cycloserine level was 91 ug./ml.

Peritoneal Dialysis

In view of her serious condition peritoneal dialysis was insti-:tuted, using Impersol-K with dextrose, 1.5% (pH 4.1). An intra-:venous infusion was also set up.

Three hours after starting dialysis the plasma cycloserine level was 65 ug./ml. and after 10 hours it was 45 ug./ml. By 20 hours the plasma level had fallen to 25 ug./ml., and the dialysis was

was stopped at 21 hours. After 17 hours of treatment the patient was much better, her level of consciousness had improved, and she was able to answer questions clearly.

At the time of her admission, 3.0 a.m. it was difficult to obtain information on the acute toxic effects of cycloserine of a level of 91 ug./ml. Peritoneal dialysis was undertaken in an attempt to improve her general condition and prevent convulsions and neuritic and circulatory complications. Only 0.53 g. was re-:covered in the dialysate but this was the minimum amount and could possibly have been more as the dialysate was not analysed for 48 hours and degradation takes place fairly rapidly in an acid medium. The clinical response, however, demonstrated that peritoneal dialy-:sis is an effective method of removing toxic amounts of cycloserine. This is the first recorded instance of peritoneal dialysis being used in cycloserine poisoning.

b) Warfarin

One patient was admitted on four occasions having taken vary-:ing quantities of Rodine, a commercial product for poisoning rats and containing warfarin. Although the prothrombin time was moderately elevated on one occasion to three times that of the control she came to no harm. A higher reading was not obtained as the poison always caused her to vomit. With Vitamin K_1 the prothrombin time reverted rapidly to normal. This was one of the very few occasions when an antidote, a true pharmacological anta-:gonist, was available.

c) Quinine

This drug still has a reputation as an abortifacient.

Frequency

Six episodes of poisoning were encountered. No adverse effects apart from the exaggerated effects of cinconism and those mentioned below were noted. It was not shown to be an effective abortifacient. In one patient severe cinconism responded rapidly to forced mannitol diuresis.

Blindness

An alocoholic male indulging in self poisoning took 60 tablets of quinine, 5 grs., blindness set in rapidly. The retinal arterioles were observed in intense spasm and remained so for many days. Retro-orbital block with Priscol (tolazoline hydrochloride) was not effective in improving his eyesight and blindness was permanent.

Cardiovascular Changes

Despite the large dose of quinine the heart showed no abnormal features apart from a persistent sinus tachycardia and considerable broadening of the Q.R.S. complexes.

Benzhezol one of the drugs employed in the treatment of Parkinson's disease has the commercial name of Artane. No instance of over-:dose by a depressed patient suffering from paralysis agitans was encountered, but Artane - known amongst the young who frequent coffee bars as R. 10 is taken for "kicks". The features produced are mood elevation with on occasions hallucinations, four instances were encountered. Treatment was but symptomatic with chlorpra-:mazine sedation.

ACKNOWLEDGEMENT

I wish to express my sincere and grateful thanks to my nursing and medical staff without whose loyal support nothing would have been accomplished.

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References

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